The New England
Journal of Medicine

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Volume 244 APRIL 12, 1951 Number 15

THE EFFECT OF ILEOSTOMY AND COLECTOMY ON THE PERSONALITY ADJUSTMENT OF PATIENTS WITH ULCERATIVE COLITIS

BENJAMIN V. WHITE, M.D.*

HARTFORD, CONNECTICUT

THE importance of psychiatric factors in ulcerative colitis is well recognized. Major contributions to our understanding have been made by Murray,[1, 2] Sullivan,[3-5] Lindemann,[6] Daniels[7, 8] and Kaufman.† Daniels has pointed out that the psychiatric aspect of the disease can most easily be comprehended through an understanding of three components: the personality make-up of the patient, environmental situations that appear to be related to exacerbations and the clinical picture, or mental status, observed during periods of severe illness. There is a remarkable unanimity of opinion on the part of psychiatrists that the personality make-up most often observed in ulcerative colitis is characterized by emotional immaturity and by inability to throw off the yoke of attachment to one of the parents or to some person serving as a psychologic substitute for one of the parents. More often than not there is a feeling of hostility or resentment toward this figure, with whom the patient lives a life of uncomfortable emotional parasitism. In our experience, approximately 50 per cent of patients with ulcerative colitis have this type of parent-dominated maturity-arrest. It is also generally agreed by psychiatrists that the environmental stimuli associated with exacerbations in ulcerative colitis are seldom calamities whose importance is obvious to the uninitiated observer. More often they are occurrences that have significance only in that they threaten a quasi-security built on immature emotional ties. According to Daniels, common situations of this type are the death of the dominant parent or parent substitute, marriage and the birth of a child.

The third component of the psychiatric aspect of ulcerative colitis, and the one with which this paper is directly concerned, is the mental status of the patient during severe illness. Again, psychiatrists are in agreement that a state of depression is most frequently observed. In our experience many of the patients also behave in a childish manner toward doctors, nurses and visiting relatives. Often they pout and whine, complain about minutiae, refuse to eat or to take their medicines and assume the totally unreasonable attitude characteristic of the spoiled child. Perhaps the words "negativism" and "petulance" describe their state well enough for statistical purposes.

Karush, in an address delivered before the American Gastroenterological Association in June, 1949, quotes Daniels as attributing the depression observed during exacerbations of ulcerative colitis to the toxicity and debility of the disease itself. The possibility that the depressed state might be caused by the diseased colon was also suggested by experience, during the recent war, with patients suffering from fulminating attacks of acute bacillary dysentery. In these patients a transient state of depression lasting for several days was not uncommon. The currently satisfactory surgical therapy of patients with ulcerative colitis affords an opportunity to evaluate the role of the diseased colon in producing the mental depression so often observed during exacerbations.

MATERIAL AND METHODS

Thirteen patients were available for study. All of these were subjected to surgery for irreversibly progressive ulcerative colitis with malnutrition. They had lost an average of 50 pounds in weight. Three had ileostomy alone, 5 had first-stage colectomy and 5 had total colectomy (Fig. 1). In all thirteen patients there was a postoperative restoration to essentially normal health, which afforded opportunity for comparison of the mental-status examination on two occasions. The patients were drawn from two hospitals. All were followed by one psychiatrically oriented internist. In a few instances the aid of a trained psychiatrist was available. The patients' life histories were studied at sufficient length for an appraisal of their ways of reacting to various situations, but no attempt at

*Assistant professor of clinical medicine, Yale University School of Medicine; chief, Gastroenterological Service, and assistant visiting physician, Hartford Hospital.

†Clinic presented before American College of Physicians, New York, 1949.

deep analysis was made. Kaufman had shown this to be undesirable during the exacerbations of ulcerative colitis.

The case history of one of the patients is recounted herewith as an example of the problem encountered.

Case History

A 30-year-old woman had her first bloody diarrhea in 1946, during the month following an attack of acute "food poisoning," which also affected her husband. She gradually went into remission and was in generally good health until June, 1947, when the diarrhea returned and necessitated hospitalization. At this time barium-enema examination revealed only minimal evidence of colitis in the sigmoid. The patient returned home, but the colitic symptoms persisted and by late August, 1947, there was a low-grade afternoon fever associated with loss of appetite and definite evidence of malnutrition. By October, 1947, the patient was extremely malnourished and showed a strong clinical and psychologic resemblance to "anorexia nervosa" (Fig. 2). She was listless, depressed, negativistic and petulant. She seemed to be on a hunger strike, for spite; her physician had considered this negativistic behavior more important than the colitis itself. When efforts at restoring her nutrition were considered hopeless, ileostomy was performed. There was gradual improvement in nutrition, morale and febrile response, but complicating arthritic manifestations were unchanged. A barium-enema examination in January, 1948, showed extensive polyposis (Fig. 3). First-stage colectomy was carried out on April 1, 1948, and the polyposis was confirmed by the appearance of the pathologic specimen. On July 1, 1948, the remainder of the colon was removed by the abdominoperineal technic. After this procedure the patient's arthritis disappeared and she became fairly well (Fig. 4). Her depression disappeared, as did the negativistic and petulant behavior, which during the illness had betrayed her immaturity. There was no fundamental change, of course, in her basic personality. The patient had considerable postoperative difficulty with prolapses of the ileostomy in August, 1948, December, 1948, and August, 1949.

At the age of 4 this patient suffered the loss of her mother. She was placed by her father in the home of a clergyman and his wife and was subsequently adopted by them. Her own father remarried, and established a home to which she never returned. The patient never felt secure in the adopted home, in which she felt she did not really belong. She had feelings of inferiority because she thought she could not live up to its intellectual and spiritual standards, and her attitude toward her own father was one of mixed emotions. With this background of insecurity, it is not remarkable that she should have become easily depressed and demonstrated immature behavior during her depression.

	Ileostomy	Colectomy
Herman	Loop	—
Casimir	End	—
Harold	End	—
Robert	Loop	Partial
Rita	End	Partial
Bill	End	Partial
Charles	End	Partial
Thomas	End	Partial
Carmelina	Loop	Total
Peg	Loop	Total
Ray	Loop	Total
Sonia	End	Total
Eugenio	Loop	Total

Figure 1. *Types of Surgical Procedure Employed in the Treatment of Ulcerative Colitis.*
All patients with colectomy had preceding ileostomy.

Figure 2. *Patient with Ulcerative Colitis in State of Extreme Malnutrition.*

Figure 3. *Roentgenogram of Colon, Showing Marked Hyperplastic Polyposis.*

Results

In some patients a good clinical result followed ileostomy alone. In most, however, persistent hemorrhagic or purulent discharge from the rectum, extensive polyposis, arthritis or some other complication necessitated partial or total colectomy. Six of the patients had personality make-ups quite like that described in the patient cited above (Fig. 5). In 4 more cases there was definite evidence of emotional immaturity, but the dependence and hostility could not be clearly demonstrated. One of the 3 remaining cases had "immaturity" that the psychiatrist was unwilling to consider abnormal. The other 2 had what appeared to be quite well

balanced personalities. As might be expected, the remissions that followed surgical intervention brought about no striking changes in the immaturity, dependency or hostility that might be considered characteristic of the personalities of the patients (Fig. 6).

Ten of the patients had periods of depression at some time during the course of the illness, some

FIGURE 4. *Same Patient, as Shown in Figure 2, Recovered from Ulcerative Colitis, Treated by Operation.*

associated with psychomotor retardation, others with apprehension and impatience. All of them were considered reactive, rather than symptoms of manic-depressive psychosis. Negativistic and petulant manifestations of childishness were encountered in 8 of the patients. These and the depressive states disappeared when, after surgery, the colonic symptoms were alleviated and the patients' nutrition was restored to normal.

Eleven of the patients returned to full normal employment, 4 as housewives, 3 as college students and 1 to each of the following occupations: chicken farmer, oil distributor, immigration inspector and guard in an industrial plant. One additional college student failed to register because of hospitalization for a prolapsed ileostomy; the 13th patient, who at one point had parenteral feeding for twenty-one days, was sent to a rehabilitation center. His

	IMMATURITY	DEPENDENCY	HOSTILITY	DEPRESSION	NEGATIVISM	PETULANCE
Peg	Yes	Yes	Yes	Yes	Yes	Yes
Sonia	Yes	Yes	Yes	Yes	Yes	Yes
Robert	Yes	Yes	Yes	Yes	Yes	Yes
Raymond	Yes	Yes	Yes	Yes	Yes	Yes
Harold	Yes	Yes	Yes	Yes	Yes	Yes
Thomas	Yes	Yes	—	Yes	Yes	Yes
Rita	Yes	Yes	—	Yes	Yes	Yes
Bill	Yes	—	—	Yes	Yes	Yes
Charles	Yes	—	—	—	—	—
Casimir	Yes	Yes	Yes	Yes	—	—
Carmelina	—	—	—	Yes	—	—
Herman	—	—	—	—	—	—
Eugenio	—	—	—	—	—	—

FIGURE 5. *Psychiatric Observations on Patients with Ulcerative Colitis.*

Immaturity, dependency and hostility are dynamic psychologic factors. Depression, negativism and petulance are symptomatic manifestations.

letters indicate that he is doing well with his program and enjoying social life.

It can fairly be said that in every depressed patient the remission that followed surgery brought relief of the depression and also a disappearance of the overt negativistic and petulant manifestations of childishness. The fundamental personality structure was, of course, unaltered.

DISCUSSION

It is perhaps useful to visualize every psychosomatic illness as a vicious cycle in which environ-

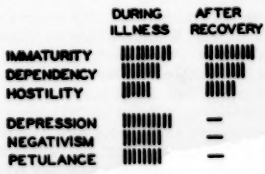

FIGURE 6. *Psychiatric Observations Made Before and After Treatment.*

Note that the symptoms of depression, negativism and petulance drop out on recovery, whereas more deep-seated immaturity, dependency and hostility remain.

mental occurrences react upon the personality to produce tension, the tension acts upon the susceptible organ to produce or aggravate disease and the symptoms produced by the disease intensify the environmental difficulties. In some psychosomatic diseases such as the toxic, febrile, debilitated phase

of ulcerative colitis, the disease may directly affect the ability of the mind to withstand disagreeable situations. The disappearance of depression and gross outward manifestations of immaturity following surgical relief in ulcerative colitis appears to break the vicious cycle and thus to bring about an amelioration of the mental status.

Does this observation have further significance in relation to the etiology of ulcerative colitis? To a certain extent, yes. In the first place, it casts doubt on the likelihood that the diarrhea of ulcerative colitis has symbolic usefulness in the sense that a hysterical paralysis does. The removal of a hysterical symptom — by hypnosis, for example — is usually followed by a new hysterical symptom. As far as is known, none of the patients reported here has developed a new psychoneurotic symptom.

In the second place, there is nothing specific about the type of personality in which emotional immaturity is coupled with dependence upon and hostility toward one of the parents. This setup is seen in the behavior problems of childhood and adolescence; it occurs with psychogenic asthma, peptic ulcer, arthritis, thyrotoxicosis and neurodermatitis; it is observed in patients with clinical psychoneuroses, and is sometimes noted in the past histories of people who are making reasonably good adult emotional adjustments.

The phenomenon that makes the personality configuration in ulcerative colitis appear specific is the commonly noted admixture of immature basic personality development with a superimposed depressive reaction. The observation of patients before and after surgical relief of the disease has made possible the differentiation of these two factors.

The factors that lead to selection of the colon as a site of disease are at present unknown, and are beyond the scope of this contribution. The concentration of lysozyme in the intestinal canal is a plausible physical explanation, but deep-seated psychologic factors cannot yet be excluded.

Conclusions

Although no specific personality type is encountered in all patients with ulcerative colitis, nevertheless many show marked emotional immaturity coupled with dependence upon and hostility toward one of the parents or some other person serving as a psychologic substitute for one of the parents.

During acute exacerbations of ulcerative colitis there is often a superadded state of mental depression in which the immaturity of the patient is brought out by childish negativistic or petulant behavior.

In thirteen patients studied, ileostomy alone, or ileostomy followed by partial or total colectomy, resulted in complete remission of the colitic symptoms, and in all cases the state of mental depression disappeared.

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FOLLOW-UP STUDY OF LUNG-CANCER SUSPECTS IN A MASS CHEST X-RAY SURVEY

CLARENCE L. SCAMMAN, M.D.*

BOSTON

THE purpose of this paper is to discuss that part of the recent Mass Chest X-ray Survey in the city of Boston that was concerned with revealing cancer of the lung. It is believed that this is the first such survey in which special procedures carried out by special staff workers have been followed to detect cancer.

The mass survey was initiated by Dr. John H. Cauley, commissioner of the Department of Health of the City of Boston, because of the high incidence of tuberculosis in the city. The survey was in operation from September 15, 1949, to February 1, 1950, with assistance, requested by Dr. Cauley, from the Public Health Service.

ORGANIZATION OF SURVEY

The first step taken in the organizing of the survey was the incorporation of a health foundation, which was planned to include most of the voluntary organizations concerned with tuberculosis and community health.

The executive committee of the foundation, made up largely of laymen, included the commissioners of the Departments of Health of the City of Boston and of the State. Its chairman was the Director of Medical Information and Education of the Massachusetts Medical Society.

This executive committee organized three divisions: Financial, Community Participation and Professional Services. The Financial Division received funds from various local organizations and disbursed them for the general purposes of the survey. The Division on Community Participation and its committees was concerned with such matters as the districting of the city, with subcommittees set up on a regional basis, to stimulate the population to have chest x-ray films taken. The usual methods of publicity were used, including newspapers and radio and fliers as well as house-to-house canvassing by local district and regional committees. A special committee concerned itself with industry.

The Professional Services Division was divided into committees responsible for the following activities: medical, nursing, social service and research. The medical committee was again subdivided into three committees: one concerned solely with tuberculosis, the discovery of new cases of which was of course the primary object of the survey, one concerned with heart findings and one concerned with nontuberculous chest diseases, which included cancer.

A roentgenological review board consisting of radiologists and chest specialists was formed by the committee on tuberculosis. This group read all large x-ray films and some small.

The chairman of the medical subcommittee on nontuberculous chest disease was a general surgeon, a member of the board of directors of the Massachusetts Division of the American Cancer Society, who selected as members seven thoracic surgeons and one internist who was especially interested in chest disease. This committee held several meetings to plan the management of the "cancer suspects." The committee was advised by several members of the medical, nursing and social-service committees.

The committee believed, in view of the urgent need of action in suspected cases of lung cancer, that follow-up by letter alone (the procedure in all other cases of chest abnormalities) was inadequate. It was decided, therefore, that each patient regarded as a "cancer suspect" should be interviewed by a medical social worker. The social worker was given the responsibility of helping the patient to secure medical study and of obtaining complete reports of the diagnostic studies.

MANAGEMENT OF PATIENTS

The routine procedure in all cases of chest abnormalities revealed by the small films was to recommend that a large film be taken. Each patient who returned by appointment for a large film was interviewed by a public-health nurse. At this interview certain specific information was added to the patient's record, including the name of the family physician, if any, or the patient's wish to be referred to a hospital or clinic.

If the large film indicated, in the opinion of the roentgenological review board, that the patient was a cancer suspect, the record was so marked by inclusion of the words "tumor suspect" as a part of the data on the film. If, as sometimes happened, the review board believed on reading the large film that the patient might have tuberculosis and cancer of the lung as well, the second diagnosis, cancer, was regarded as having priority. The record was then referred to the medical social worker for follow-up study.

At the interview with the patient the social worker explained that although a shadow appeared in the large film no definite diagnosis could be made on this evidence alone and advised further study by a physician. The social worker explained her responsibility to the patient and gave him an opportunity to ask questions and to discuss his own situation

*Medical director, American Cancer Society (Massachusetts Division), Inc.

before the means of obtaining a more complete diagnosis was discussed. Naturally, many patients had emotional reactions of greater or lesser degree. The social worker did her best to meet these problems, as well as others that the patient presented during the interview. Those patients who said that they wished to consult their family physician were urged to see him at once, and a report of the reading of the film was sent to him immediately. In addition, the physician was frequently informed by telephone that the patient was coming and was asked whether or not he wished to have the film itself. The large film was made available to any physician on request. In many instances the family physician asked for assistance in making arrangements for his patient to be studied at one of the city's several thoracic clinics. It is of interest to note here that few patients who had no private physician asked to be referred to one.

Patients in need of referral to a clinic or hospital were given information about those available. The suitability of these clinics for the individual patient was discussed with him; when necessary he was helped to make a decision. Usually a clinic appointment was made for the patient before the interview ended, and he was given a note of introduction to the social worker in the hospital clinic. When the report on the large film was sent to the hospital it was accompanied by a letter giving social information obtained in the interview with the patient and calling attention to any special problems that had been uncovered that might complicate the patient's treatment.

Intensive follow-up studies were carried out on all patients, both those studied at clinics and those under the care of private physicians. The social worker was in close touch with all hospital social workers. If the patient failed to keep his clinic appointment, the social worker undertook the responsibility for further follow-up of the patient. In most cases, after the patient had made one visit to the clinic further follow-up responsibility was assumed by the hospital social worker. To obtain reports of final diagnoses, necessary contacts were made with both doctors and clinics to assure results.

The physicians in the area, with few exceptions, were actively interested in further studies on their patients and in reporting their findings.

Because of the urgent need of the diagnosis, efforts were made to interview the patients as soon as possible after the reading of the large film and to help them secure additional medical advice at the earliest possible moment. The time involved in these procedures is not available in every case. However, the available facts concerning the proved primary cases are as follows*: The median period from the reading of the large film to the interview with the social worker was fourteen days; the median period from the interview with the social worker to the patient's first visit to the doctor was five and a half days; the median period from the first visit to the doctor to the establishing of the diagnosis was twenty-four and a half days. The over-all median period from the reading of the large film to the establishing of the diagnosis was forty-four days.

Because the date of the original small film was not included on the record, it is impossible to estimate the elapsed time between the taking of the film and a diagnosis of the case. Experience with this study leads us to believe that about two weeks should be added to the time indicated above (forty-four days) between the reading of the small film and the establishing of a diagnosis, making a total of fifty-eight days.

TABLE 1. *Incidence of Cancer of the Lung in Mass Chest X-ray Survey.*

Total small films			536,012
Total large films			9372
Total large films showing thoracic abnormalities			7254
Total large films classified as suggestive of cancer		398*	
Total diagnostic reports received		343†	
Patients with diagnoses other than cancer	267		
Diagnoses of cancer	76‡§		
Proved primary cancer	43		
Other types of malignancy	3		
Metastatic cancer	15		
Presumptive diagnosis of cancer	15		
Patients on whom reports pending		12	
Patients on whom no reports received		43	

*74.2 per 100,000 small films.

†85.9 per cent of total cancer suspects.

‡14.2 per 100,000 small films.

§Nine additional cancer cases not included in the 398 cancer suspects — total cancer cases 76 plus 9, or 85; new rate, 15.8 per 100,000 small films.

DISCUSSION OF THE PERSONS CONSIDERED CANCER SUSPECTS

Table I summarizes the pertinent facts in this study. Five hundred thirty-six thousand and twelve small films were taken in the survey; of these, 398, or 74.2 per 100,000, were finally determined on the reading of the large film to be cancer suspects. Diagnostic reports were received on 343 of these 398 cases, or 85.9 per cent. Of these 343 cases, 267 were finally reported as having chest conditions other than cancer, or as having no disease.

The remaining 76 persons were reported to have cancer.† Of these, 43 were proved to have primary cancer of the lung (7.8 per 100,000). Three other types of malignancy were uncovered: 1 lymphoma, 1 lymphosarcoma and 1 Hodgkin's disease. Fifteen subjects had metastatic lesions in the lung; in fifteen others the presumptive evidence indicated cancer. Study of these last 15 cases, although not diagnostically conclusive, was extensive enough to

*These figures are based on 44 cases: 41 of proved primary cancer and 3 of other types of malignancy. Although 43 cases of primary cancer are discussed in the text, 2 cases were omitted here because the lesion was known to the patient's physician before the survey film was taken, and no action was taken in regard to further medical follow-up.

†Cases of adenoma of the lung, of which there were 5, are not included in the cancer group.

warrant the presumption of cancer. Of the 43 primary malignancies, pneumonectomy or lobectomy was performed on 20 patients. Twenty-one cases were inoperable*; 2 patients refused surgery. Of the 15 patients regarded on presumptive evidence as having cancer, 7 refused further study; no further investigation was advised on 6; 1 is still under observation; and 1 died before diagnosis could be proved. As of July 31, 10 cases diagnosed as primary, 2 with metastases to the lung and 1 case diagnosed as presumptive were known to have terminated fatally.

Of the 398 cancer suspects, 216 were referred to private physicians; 47 of these patients were subsequently sent by their physicians to a hospital or clinic for study and treatment. One hundred and seventy-nine of the 398 went to hospitals or clinics; 19 of these consulted private physicians after an initial visit to a hospital or clinic. The remaining 3 were referred to neither physician nor hospital because they did not respond to any follow-up, and it was impossible to obtain any action from them.

No diagnostic reports were received on 55, or 14.1 per cent, of the 398 cancer suspects. Of these 55 patients, 12 carried out the recommendations that they have further medical study. However, there is no final report on these, either because diagnosis had not been reached at the time the study was completed or because the doctor failed to report his findings. In the other 43 cases, 18 patients failed to consult a doctor or clinic at all, and 25 made an initial visit to a doctor or clinic but refused to carry out additional study as advised.

Two hundred and sixty-seven of the 398 cancer suspects are not discussed here because 253 fall into the category of chest conditions other than cancer and 14 had no chest disease. Of the 267 diagnoses of patients with chest conditions other than cancer, the majority fell into the following categories: tuberculosis — active, inactive and healed, benign tumor, tuberculoma, substernal goiter, cyst and bronchiectasis.

In addition to the 398 cancer suspects discussed in detail in this paper, 9 additional cases of cancer were discovered in the final analysis of survey films, as detailed below. These films were originally read as tuberculosis or nontuberculous lesions. Three of the 9 had small films only, and 6 had large films. Further medical study of these patients resulted in reports of 2 cases of primary cancer of the lung, 3 of presumptive cancer of the lung, 1 of definite metastasis and 3 of suspected metastases.

In spite of the fact that these 9 cases were not included in the detailed study, it is evident that they should be a part of the total picture. Table 1 shows against the item "Total diagnoses of cancer," by means of a footnote, how these additional 9 cases affect the total rates.

*Exploratory thoracotomy was performed in 8 of these cases.

Discussion of Tables

A brief discussion of Tables 2 and 3, namely, total cancer suspects by age and sex and persons diagnosed as cancer by age and sex, follows. No figures are available by age and sex for the over-all survey against which the figures in Tables 2 and 3 could be projected.

A comparison of Tables 2 and 3 shows that there were 26 cancer suspects under the age of 30, only 1 of whom was found to have cancer. Also, in Table 2 the group of cancer suspects between the ages of 50 and 69 includes 215, or 54 per cent of the total cancer suspects. Table 3 shows that in this same age group, 50 to 69, there were 52 persons, or 68 per cent of the total cases, diagnosed as cancer.

Table 2 shows that of the 398 cancer suspects, 235, or 59 per cent, were males and 163, or 41 per cent, were females. Table 3 shows that of the 76 persons diagnosed as having cancer, 54, or 71.0 per cent, were males, and 22, or 28.9 per cent, were females.

Table 2. *Cancer Suspects, by Age and Sex.*

Age	M	F	Total
Under 15	1	0	1
15–19	4	2	6
20–29	9	10	19
30–39	16	18	34
40–49	32	38	70
50–59	62	43	105
60–69	75	35	110
70–79	29	17	46
80–89	7	0	7
Total	235	163	398

Table 3. *Cases Diagnosed as Cancer, by Age and Sex.*

Age	M	F	Total
Under 15	0	0	0
15–19	1	0	1
20–29	0	0	0
30–39	3	1	4
40–49	2	6	8
50–59	20	5	25
60–69	21	6	27
70–79	5	4	9
80–89	2	0	2
Total	54	22	76

A breakdown of those persons with primary cancer (46) and those with metastases (15) shows in the first instance 35 men, or 76.1 per cent, and 11 women, or 23.9 per cent, with primary cancer, and in the second instance 6 men, or 40 per cent, and 9 women, or 60 per cent, with metastatic cancer.

Cost of Follow-up of Cancer Suspects

The primary expenditures were for the employment of two medical social workers, one for a period

of nine months and one for a period of three months, the first of whom worked four days a week and the second of whom worked three days a week. A full-time secretary was employed for the nine-month period. Costs for salaries of these three workers were $3716. The cost of telephone service was $103. Expenditures for stationery, stamps and other office supplies were estimated at $50. Rent for 3 desks and 1 typewriter was $166. Space for these workers was provided by the survey organization. The total cost itemized above is $4035. The only item not based on accurate figures is that concerned with costs for stationery, stamps and other office supplies. From time to time during the study the main office of the American Cancer Society furnished office supplies and stamps not charged directly to this study. Nevertheless, it is believed that the estimate of $50 is reasonably accurate. Moreover, survey headquarters mimeographed form letters without charge and made other contributions, particularly through its general records office, the costs of which were absorbed by the general survey.

Based on the total cost of $4035, the follow-up of 398 cancer suspects represents an individual cost per case of about $10. If the total cost is charged against the 76 cancer cases only, then the cost per cancer case is about $53.

Although the medical social work involved was primarily concerned with service to the patient, a great deal of time was expended in securing reports on individual cases and in making full and accurate records of all the information available about each individual patient. Obviously, without this detailed information the report on this study would have been impossible.

Discussion

The subcommittee on nontuberculous disease, concerned essentially with cancer and comprising principally thoracic surgeons, as mentioned earlier, was appointed about October 1, 1949. Plans set up by this committee were not put into effect until a medical social worker with both academic training and broad experience was finally secured on November 1. This was six weeks after the survey started. This delay was regrettable, because many policies and details of the work were not formulated until after November 1, and as a result the actual interviewing of patients got under way more slowly than was desirable. Moreover, a number of cases had accumulated in the short period before the social worker began work, which increased the number of patients for whom interviews had to be scheduled immediately. Those subjects who had been suspected as having cancer in the first five weeks of the survey had been already advised by letter to secure further medical study and were not interviewed by the social worker. These patients, however, were followed later in order to obtain diagnostic reports and are included in the figures of the study.

In any future survey, an effort concerned with the follow-up of cancer suspects should be planned well before the start of the survey. This should include the creation of a responsible committee, the employment of necessary personnel and the formulation of detailed plans. Some one person should be responsible for the supervision of such a program.

Summary and Conclusions

The American Cancer Society (Massachusetts Division), Inc., employed social workers and a secretary to study and follow up the tumor suspects found in the mass chest x-ray survey carried out in Boston in late 1949 and early 1950. In the course of the survey 536,012 subjects were examined. Three hundred and ninety-eight films were originally classified as suspected cancer. A diagnosis of cancer was made in 76 cases. Primary cancer was proved in 43, and radical operations in an attempt at cure were performed on 20.

The cost of salaries and the expenses of workers employed by the Cancer Society was $4,035, so that the cost of this item for the 76 patients was $53 per patient. If the entire cost is charged against those patients who had a chance of surgical cure, this item amounts to $200 per patient. This additional effort, made for the first time in such a survey, is considered to have been well worth while.

CAT-SCRATCH FEVER

A Disease Entity*

WILLIAM E. R. GREER, M.D.,† AND CHESTER S. KEEFER, M.D.‡

BOSTON

THE domestic cat has long been known as a carrier of disease. Unfortunately, perhaps, cats have long enjoyed intimate companionship with human beings and their households. Many homeless cats are accepted in homes out of sympathy, with no investigation or consideration of their disease status. The occurrence of a disease entity incurred through cat scratches in a young adult male has prompted this report.

There are no reports in the English literature concerning "cat-scratch fever."§ It is a term first used by Dr. Lee Foshay,[1] of Cincinnati, to describe lymphadenitis of unknown etiology following cat scratches. The disease is suggestive of, but much milder than, tularemia. A cat contact is invariable. Although it is a systemic disease associated with malaise, fever and other general symptoms of an infection, the brunt of the infection is borne by lymph nodes. Symptoms referable to other systems are usually minor and transitory. Occasionally, as in our case, exanthems occur, resembling erythema multiforme. The case herein reported is the first to have exhibited erythema nodosum. There are no characteristic clinical or laboratory findings, except those that exclude adenopathy of known etiology. The infective agent has never been identified; it is apparently a virus. An agent is present in the pus from buboes and produces a specific skin reaction after it has been made into a skin antigen by the classical Frei procedure and injected intradermally into the patient. The disease is a self-limited one; thus far no specific therapy is indicated.

Debré and his co-workers[2] have recently described this disease syndrome in the French literature under the name "La maladie des griffes de chat." These authors stated that they had studied 10 such cases but reported in detail only 1 case. They also noted a positive reaction to Foshay cat antigen and believed it to be specific. In their case report, a 6½-year-old child developed the syndrome of fever, inguinal adenopathy and local folliculitis after contact with a cat. Penicillin had no effect on the course of the disease, but it was their belief that aureomycin shortened the course of the illness.

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Instructor in medicine, Boston University School of Medicine, and assistant member, Evans Memorial, Massachusetts Memorial Hospitals.

‡Wade Professor of Medicine, Boston University School of Medicine, and director, Evans Memorial, Massachusetts Memorial Hospitals.

§We are grateful to Dr. Lee Foshay for calling our attention to the occurrence of this disease, and for the antigen that was used to test this patient.

CASE REPORT

A 36-year-old white man was admitted to the Evans Memorial Hospital on March 7, 1950, with a chief complaint of glandular swelling in the neck and rash on the arms of two weeks' duration.

His past history was not remarkable, other than that six years prior to admission the patient had an episode of glycosuria, with a negative glucose tolerance test. He had had frequency of urination with the present illness.

The patient was apparently well until about two weeks prior to admission. At that time he awakened one morning to find his house cat (a homeless stray cat) licking the left side of his neck in an area that contained two pimples. He was scratched on the right hand at about the same time. Ten days prior to admission the patient noted a painless swelling of a gland on the left side of his neck. The swelling increased to the size of a hen's egg. Seven days prior to admission he felt weak, tired and somewhat chilly. The patient visited his local physician, who treated him with 600,000 units of penicillin and advised warm, moist dressings on the glandular area. Malaise increased; on the third day prior to admission the patient had a shaking chill. His temperature was 101° at that time, and his physician again administered penicillin. The neck gland was incised, but there was no drainage. Two days before admission the patient noted the onset of a pinkish macular rash over the extensor surfaces of his arms that gradually developed into small vesicles. On the day prior to admission the temperature was elevated to 101°, the above symptoms continued and in addition a tender, reddish, raised nodule surrounded by an erythematous area developed on the anterior surface of the right tibia. Hospitalization was advised.

Physical examination revealed a well developed and nourished young man, who seemed flushed and acutely ill. The temperature was 101°, the pulse 100, the respirations 18 and the blood pressure 140/100. His skin was warm and moist. There were bright-pink macular, raised eruptions over the extensor surfaces of the upper extremities, 1 by 1 cm. in size, approximately 60 in number. These lesions were topped by small vesicles. On the anterior surface of the right tibia was a raised, warm, poorly circumscribed pinkish nodule, 1 by 2 cm. in diameter, surrounded by an erythematous area. At the angle of the left mandible was a warm, large 5-by-4 cm. glandular swelling, which was tender and had a healing operative incision. Beneath this gland was a 1-by-2 cm. firm, freely movable, nontender gland on the lateral aspect of the cervical region. Other mild adenopathy was noted in both axillary areas and the left supraclavicular area. The bones, joints and muscles were not remarkable. The eyes were normal. Both pupils reacted to light and accommodation. The ears, nose and throat revealed no inflammation or other abnormality. The chest was clear to percussion and auscultation. The heart was normal. Genital and rectal examinations were negative. Neurologic examination was within normal limits.

A blood Hinton test was negative. The urine was normal. The hematocrit was 46 per cent, and the hemoglobin 15 gm. per 100 cc. The white-cell count was 10,200, with 92 per cent neutrophils and 8 per cent lymphocytes. Repeated white-cell counts ranged between 10,000 and 6100, with 58 per cent neutrophils, 38 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. The sedimentation rate was 33 mm. per hour on admission, falling to 8 mm. per hour. The nonprotein nitrogen was 32 mg. per 100 cc. The fasting blood sugar was 119 mg. per 100 cc. on two occasions. An oral glucose-tolerance test was of the diabetic type. Nose and throat cultures were negative for pathogens. Tularemia-agglutination tests were negative. Smears from the gland drainage were negative for acid-fast bacilli. Cultures from the gland grew out a few colonies of weakly pigmented *Staphylococcus aureus*. Repeated blood cultures showed no

growths. The Frei test was negative on two occasions. X-ray examination of the chest was within normal limits.

The patient had temperature elevations to 102° for the first three hospital days and became afebrile after the fifth hospital day. On the fourth hospital day the patient's neck gland spontaneously drained. It was cultured and a skin antigen prepared from the material by the classical Frei procedure. On the sixth hospital day the drainage stopped, and it was noted that the skin rash was beginning to fade. During the hospital course there was a gradual reduction in the size of the neck gland, and the patient rapidly became asymptomatic.

Results of Intradermal Antigen Studies

Dr. Lee Foshay, of Cincinnati, supplied us with a vial of "cat fever" antigen prepared from a former patient's bubo, heated to 60°C. for two hours on one day and for one hour on the next day, after

FIGURE 1. *Elevated Macular Eruption That Appeared on Twelfth Day of Disease.*

1:1 dilution with sterile salt solution. An intradermal injection of 0.1 cc. was given to the patient on the sixteenth day. At twenty-four hours there was itching, redness and swelling at the site of the injection over an area of more than 3 cm. in diameter. At forty-eight hours the reaction was maximal and persisted for a few days thereafter. The antigen was tested on 6 control patients; no reaction was noted. Frei antigen and saline were used as controls. As noted above, an antigen was prepared from the material in our patient's neck bubo in the manner described for Frei antigen preparation and 0.1 cc. was injected intradermally. A positive reaction was noted at twenty-four hours and forty-eight hours with redness, swelling and slight itching over an area more than 2 cm. in diameter. Six control patients showed no reaction to intradermal injection of this material. These results seem to indicate a high specificity of this antigen.

DISCUSSION

It is of interest to note, in Defoe's "A Journal of the Plague Year,"[3] which appeared in 1722, that the possible dangers of disease transmission by cats were recognized and that drastic extermination measures were carried out. The following excerpt is quoted: "Wherefore, were we ordered to kill all dogs and cats: but because as they were domestick animals and are apt to run from House to House, and from Street to Street, so are they capable of carrying the Effluvia or infectious steams of the bodies infected, even in their furrs and hair; and therefore, it was that in the beginning of the infection, an order was published by the Lord Mayor, and by the Magistrates, according to the Advice of the Physicians, that all the dogs and cats should be immediately killed, and an officer was appointed for the execution."

It seems that present dangers of disease transmission by house cats are not well recognized. Table 1 lists the diseases of human beings that are found in cats and those diseases that have been transmitted by cats to man. This is a formidable list. Since the cat, as well as other animals, shares many diseases or parasites with man, it is a reservoir

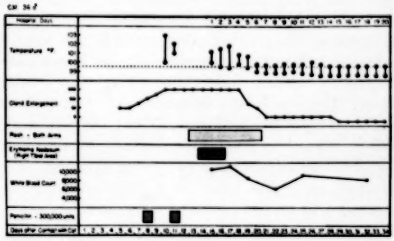

FIGURE 2.

host. Transmission of the disease to man depends on environmental factors and type of contact.

Tularemia has been reported by many authors[4-6] as having been contracted through the bite of the domestic cat. This transmission is of a more mechanical nature, since the organisms may be present on cats' teeth after they have eaten infected animals. Rudesill's case[5] was of interest in that a woman was bitten by a nursling kitten of a cat that became ill after having killed and partly eaten a rabbit. Three days after the kitten's bite, the patient developed proved tularemia. The kitten and a litter mate died about six days after infection; the mother cat slowly recovered.

Rabies is not uncommonly found in cats, and a rabid cat is a serious menace to human beings. Cats may harbor this disease through their close contact with dogs and other lower animals that may have rabies. Stimson[7] reported that of 588 animals diagnosed as positive for rabies over a ten-year

period thirty-four were cats. Hull[8] reported that at the laboratory of the Illinois State Department of Public Health there were 416 positive animal heads over a four-year period, of which 18 were of cats. The incubation period was reported as fourteen to sixty days. Hull[8] states that the rabid cat hides itself in dark areas and comes forth for vicious attacks. The animal loses its voice and mews hoarsely. Later the appetite is lost, and there is progressive emaciation, paralysis and death.

Cat-bite fever and rat-bite fever are the same disease. The disease, also known as Sodoku (rat poison), occurs all over the world. Beaumont and Gill[9] have reported a case of rat-bite fever developing in a 14-year-old girl after she was bitten by a stray cat. The causative organism was not recovered, but features of special interest in this case included recurrent fever with rash, localized muscular swellings, conjunctivitis and a positive Wassermann test. Collier[10] noted 2 cases of rat-bite fever following cat bites, in one of which gland puncture demonstrated spirochetes. Both cases were characterized by recurrent episodes of fever associated with purplish macular eruption and lymphadenopathy. There was good response to novarsenobillon therapy.

Feline virus pneumonia and its possible relation to some cases of primary atypical pneumonia in man have been reported by Blake and his co-workers.[11] A young farmer had been admitted to the New Haven Hospital with an illness resembling primary atypical pneumonia of presumed virus etiology. Further history revealed not only that two other members of the household had had a recent similar illness and that another was ill at home but also that one month previously 8 of their 12 cats had died of an acute respiratory disease characterized by mucopurulent conjunctivitis, rhinitis, sneezing and coughing. Two of the remaining four cats were ill with the same disease. The possibility suggested itself that the afflicted members of the family and the cats were infected with the same agent, and an investigation was carried out. A virus capable of producing a similar pneumonia in other cats (particularly kittens) was recovered from the lungs of one of the family cats. The histologic characteristics of the pulmonary lesions in the cats, particularly the necrosis of the bronchiolar and alveolar epithelium, the predominant large-mononuclear-cell reaction early in the disease and the absence of pleural reaction pointed to a virus etiology. One of our staff physicians mentioned an instance occurring this past winter in which the family kitten developed an upper-respiratory infection characterized by frequent sneezing. The kitten sneezed in a child's face several times, and subsequently several members of the household developed upper-respiratory infections. No studies were carried out in this instance.

Diphtheria has long been suspected, even by lay persons, as being carried by the domestic cat. Simmons[12] noted that Karbinski in 1908 reported an outbreak of diphtheria in 24 Angora cats, with 17 deaths. Karbinski further reported diphtheria in children infected after contact with cats.

Tuberculosis is uncommon among cats, especially in the United States.[8] In European cats the incidence of infection varies with geographic location and is dependent on the prevalence of tubercle bacilli in the milk supply, but averages about 2 per cent. Cats are resistant to human and avian types but are susceptible to the bovine type, with the digestive tract as the usual portal of entry. Hull[8] quotes Dobson[13] as having observed bovine tuberculosis in 11 of 505 cats examined in Edinburgh. The most common characteristic was emaciation. The disease process is usually of the miliary type. Open cutaneous lesions may occur; they are a potential source of tuberculosis to man, since these lesions contain numerous tubercle bacilli.[14] The first case in which a human being was undoubtedly infected by a diseased cat was reported by Lewis–Jonsson.[15] A 3-year-old boy had been bitten on the right forearm by a cat that was found dead two days later. Within a month the cutaneous wounds became infiltrated and enlarged. Axillary adenitis and fever developed. A chest roentgenogram showed bilateral infiltration. The child died of tuberculous meningitis after three and a half months. Post-mortem examination showed ulcerative tuberculosis of the skin of the forearm and miliary and meningeal tuberculosis. Guinea-pig inoculation and cultures showed the bovine type of tuberculous bacilli.

Brucellosis is another common disease that may be transmitted by cats. Bruce[16] found in 22 cats 5 positive reactions; he isolated *B. melitensis* from the mesenteric lymph nodes of one.

At least 5 cases of typical murine typhus, including 1 laboratory infection probably acquired through the agency of cat fleas harbored by kittens obtained from a Texas feed store, were reported by Irons and his co-workers.[17] It might be postulated that the fleas in question had acquired the infective agent from the kittens. Fleas were taken from two litter mates of the involved kittens, and typical murine typhus was obtained in male guinea pigs by inoculation of suspensions of *Ctenocephalides felis*, the cat flea. Irons[17] further quoted Lepine and Lorando[18] as having produced experimental infections in cats — usually of the inapparent type.

It is possible that cats may harbor spirochetes of leptospirosis as a result of eating infected rats. One might therefore be particularly wary of cats that frequent slaughterhouses, fisheries and similar areas.

Ringworm may be transmitted by cats. Roberts[19] reported a kitten that infected thirteen human beings with *Microsporum felinum* and also infected another kitten, which in turn infected a child and a dog. Other types of ringworm that may be ac-

quired from cats are ringworm of the glabrous skin (*Trichophyton circinata*) and favus, a scalp infection caused by *Achorion schoenleini*, acquired by cats from rats.[7]

Creeping eruption, caused by *Ancylostoma braziliense*, may be carried by cats. It has been suggested that cats be kept from places where people may go barefoot.

Pasteurellosis following car-bite and scratch wounds has been reported in man. Hansmann and Tully[20] reported two pasteurella infections and one reinfection in man following cat-bite and scratch wounds. A gram-negative organism of the genus *Pasteurella* was isolated in each case. Allott and

Table 1.

Diseases Transmitted by Cats to Man
Tularemia
Rabies
Rat-bite fever
Feline pneumonia (virus)
Diphtheria
Tuberculosis
Brucellosis
Typhus
Leptospirosis (?)
Ringworm (*Microsporum felineum, T. circinata*)
Creeping eruption (*Ancylostoma braziliense*)
Favus (*Achorion schoenleini*)
Pasteurellosis
Plague (?)
Histoplasmosis (?)
Cat fever
Human Diseases Found in Cats
Tuberculosis (bovine)
Tularemia
Ringworm
Amebiasis
Diphtheria
Salmonellosis (*S. enteritidis, S. anatum*)
Brucellosis
Rabies
Favus
Trypanosomiasis (*T. cruzi*)
Leishmaniasis
Creeping eruption
Dog tapeworm (*D. caninum*)
Fish tapeworm (*D. latum*)
Lung-fluke disease (*P. westermani*)
Opisthorchiasis
Schistosomiasis japonicum
Strongyloidiasis
Spirillosis
Scrub typhus

his co-workers[21] reported 3 cases following cat-bites, with isolation of the gram-negative coccobacillus *Pasteurella septica*. The organism inhabits the human respiratory tract, as well as that of lower animals. Cellulitis with regional lymphadenitis characterizes the infection.

Histoplasmosis has been reported as occurring spontaneously in 3 dogs and a cat; this fact appears to indicate these animals as of possible importance as a source of human infection.[22] Callahan[22] suggests that since a large number of the cases of histoplasmosis in the St. Louis areas have been in children who had been in close contact with pet animals it is of some importance to recognize the disease as occurring in animal reservoirs. Summerhill[23] identified intracellular parasites considered to be Histoplasma in the lungs and mesenteric lymph nodes of a cat. It has been suggested[22] that, since the reported occurrence of histoplasmosis throughout the world is small, man-to-man transmission is unlikely and there may be an outside reservoir of the disease. The respiratory and gastrointestinal tracts have been suggested as the portals of entry.

Many animal parasites are found in domestic cats (Table 1), but most of these are of small epidemiologic significance.

Lay persons and physicians not infrequently speak of "blood poisoning" following cat scratches. It is possible that this septicemia may represent "cat-scratch fever."

Summary

A case report of "cat-scratch fever" is presented. The disease is characterized by a history of previous domestic cat scratches followed by a systemic infection with malaise and fever in which the brunt of the infection is borne by the lymph nodes. Occasionally, lesions similar to exanthems or erythema nodosum may occur. The infective agent has never been isolated but is apparently a virus. The agent is present in the pus from lymph nodes involved and produces a specific skin reaction when made into an antigen. No specific therapy is indicated at present.

A review of diseases that may be transmitted to human beings through cat contacts is presented.*

*Dr. Franklin Hanger has called our attention to cases of suppurative lymphadenitis in which there has been no previous contact with cats but in which the infected patient reacts with a positive skin test to his own pus. Material obtained from Dr. Hanger from such a patient failed to cause a reaction in our patient, and our antigen failed to cause a positive skin reaction in a patient who had had an attack of suppurative lymphadenitis unassociated with cats.

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SEVERE HYPOPROTHROMBINEMIA FOLLOWING PROPYLTHIOURACIL TREATMENT OF THYROTOXICOSIS*

CHARLES G. CRADDOCK, JR., M.D.,† DONALD SHOTTON, M.D.,‡ CHARLES L. CROCKETT, M.D.,§ AND BYRD S. LEAVELL, M.D.¶

CHARLOTTESVILLE, VIRGINIA

THE following report concerns a case of severe hemorrhagic diathesis appearing during the course of propylthiouracil treatment of thyrotoxicosis. The fundamental defect was a marked prolongation of the prothrombin time, transient in nature. The case is unusual in two respects. First, the prothrombin deficiency occurred as an isolated phenomenon without evidence of liver damage or depression of white blood cells; second, the hemorrhagic tendency was quickly ameliorated by the administration of fresh homologous human serum and whole blood.

CASE REPORT

E. L. M., a 16-year-old schoolgirl, was admitted to the University of Virginia Hospital June 10, 1949, because of profuse epistaxis.

The patient had been well until January, 1949, at which time she became excitable. Subsequently there was noticeable swelling in the region of the thyroid gland, with prominence of the eyes. Associated symptoms were a lack of interest in her schoolwork, markedly increased appetite with a weight gain of about 1 pound a week, palpitations and exertional dyspnea. Menses started in January, 1949, and the patient experienced short periods (of two days' duration) with scanty flow at monthly intervals.

She consulted her local physician on February 4, 1949; he started treatment with thiouracil, 150 mg. per day in divided doses, later increasing the dose to 300 mg. per day. The basal metabolic rate on February 19 was + 42, later falling to + 25 and + 15 on March 5 and March 12 respectively.

The patient was admitted to Walter Reed General Hospital on March 23. At this time previous medications were stopped. Signs of thyrotoxicosis continued, including widening of the palpebral fissures, tachycardia and a diffusely enlarged thyroid gland with a detectable thrill and bruit. The basal metabolic rate on April 4 was +8. Blood counts revealed no anemia or leukopenia. The white-cell count varied between 3600 and 7000, with not less than 45 per cent polymorphonuclear leukocytes. Certain liver-function tests, including thymol turbidity, serum protein, albumin-globulin ratio and cephalin flocculation, were normal. The blood cholesterol was 115 mg. per 100 cc. The 17-ketosteroid excretion was 5.051 mg. per twenty-four-hour specimen.

The basal metabolic rate steadily increased while she was under observation. On May 8 she was started on 300 mg. of propylthiouracil daily, in three divided doses. The only other medications were phenobarbital, 65 mg. daily, and ferrous sulfate. She was discharged on May 31, 1949, and because of a change of address was instructed to report to the University of Virginia Out-Patient Clinic for further treatment.

When first seen at the University of Virginia Hospital on June 11, 1949, she had been suffering from intermittent epistaxis for three days. The bleeding had been continuous and profuse for the previous twenty-four hours. An abrasion of the left forearm also oozed blood steadily.

She denied any previous bleeding phenomena. The last menstrual period had ended two weeks before admission and had been normal in duration and amount. There were no pertinent illnesses in the past medical history; review of the systems, other than symptoms referable to the hyperthyroidism, was negative.

There was no history of contact with or ingestion of known clotting inhibitors, nor was any illness suggestive of liver disease elicited. She mentioned that she had once had jaundice as an infant. The family history was negative for any hemorrhagic diathesis. The father and mother both had normal prothrombin times on examination in our laboratory. There were no siblings.

Physical examination revealed a well developed young girl, slightly obese (weighing 147 pounds). The temperature was 100.4°F., the pulse 114, and the blood pressure 140/70. The thyroid gland was diffusely enlarged and smooth, with no detectable thrill or bruit. There was no tremor, but the palpebral fissure was widened and there was definite lid-lag.

Scattered pin-point petechiae (3 to 4 per square inch) were present over both lower extremities. Blood was flowing from the nostrils, and there was oozing of blood from the gums and the abrasion of the left forearm. An ecchymotic area, 4 cm. in diameter, covered the left elbow. No jaundice was noted. Aside from an apical systolic murmur the heart was normal. The spleen and liver were not palpable; no significant lymphadenopathy was noted.

Laboratory studies revealed very slight anemia, the red-cell count being 4,200,000, the hemoglobin 12 gm. per 100 cc. and the hematocrit 36 per cent. The white-cell count was 12,300, with 76 per cent polymorphonuclear lymphocytes, and a normal differential smear. The blood coagulation time (Lee–White) was forty minutes. Testing for the presence of an anticoagulant, by adding varying amounts of normal blood to the patient's blood, was negative. The prothrombin time‖ was 200 to 230 seconds with a control of twelve seconds. This value was obtained three hours after 70 mg. of vitamin K had been administered intravenously. Bleeding time, capillary fragility test, platelet count and clot retraction were all normal.

Liver-function studies showed no other abnormalities; the cephalin flocculation was ±, the thymol turbidity 1.1 units, the icteric index normal, the cholesterol 195 mg., the total proteins 6.7 gm. and the fasting sugar 99 mg. per 100 cc. The glucose-tolerance curve was normal.

Roentgenograms of the chest and abdomen were normal. The bones of the wrist and hand showed normal epiphyseal development for the patient's age.

Hospital course. Because of the alarming hypothrombinemia and persistent hemorrhage from multiple sites, all medications were discontinued at the time of admission. Bleeding occurred at the site of venipunctures and could not be controlled by pressure dressings. The epistaxis was not controlled by packing or cauterization. Seventy mg. of vitamin K, given parenterally at the time of admission, had no immediate hemostatic effect.

Fresh thrombin-free serum was prepared by removing the serum layer from homologous clotted blood after centrifugation. After intravenous administration there was a fall in the prothrombin time to twenty-seven seconds in one hour. By the use of repeated injections of fresh serum and whole

*From the Medical Service, University of Virginia Hospital.

†Formerly, instructor, Department of Medicine, University of Virginia; Markle Foundation Scholar in Medical Science; teaching fellow in psychiatry, Massachusetts General Hospital.

‡Formerly, assistant resident in medicine, Department of Medicine, University of Virginia; resident in internal medicine, Joseph H. Pratt Diagnostic Hospital, Boston.

§Formerly, fellow in medicine, Department of Medicine, University of Virginia; Damon Runyon Fellow in clinical research, Evans Memorial, Massachusetts Memorial Hospitals, Boston.

¶Associate professor of internal medicine, Department of Medicine, University of Virginia.

‖Prothrombin time determined by the Quick method, performed at 37°C., with freshly prepared active rabbit-brain thromboplastin.

blood, the bleeding tendency was kept under control. The details of this therapy are presented in Figure 1. After the first day and a half of hospitalization there was no further abnormal bleeding. On the sixth hospital day the patient began menstruating. The period was of the usual duration and amount for the patient.

The readministration of propylthiouracil was considered in order to establish the toxic relation of this drug to the

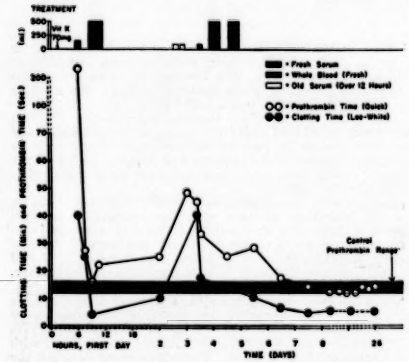

FIGURE 1. *Effect of Intravenous Serum and Blood on the Patient's Prothrombin and Clotting Time. Note the marked response following fresh serum alone.*

hypoprothrombinemia. This was deemed too hazardous in view of the serious thyrotoxic status of the patient and was not carried out.

The temperature curve, which was spiking to 102°F. for the first four days, gradually declined and was normal after the sixth day. The pulse rate remained rapid and labile, and the patient still exhibited signs of thyrotoxicosis. Consequently, on the ninth day phenobarbital (16 mg. four times daily) and Lugol's solution (5 drops three times daily) were initiated. No toxic reactions were noted. Because of the inability to control the hyperthyroidism, particularly since the thiourea derivatives seemed contraindicated, surgical intervention was decided upon. The prothrombin time remained within normal limits and no further bleeding phenomena occurred. The patient was thought to be in good preoperative condition.

On July 1, 1949, a subtotal thyroidectomy was carried out. No unusual degree of bleeding was encountered; postoperative wound healing was rapid and the clinical course was one of steady improvement. The excised portion of the thyroid gland was slightly nodular in appearance. At histologic examination the acini were small and the lining epithelium was tall and columnar in many areas. There was moderate scarring and lymphocyte infiltration of the gland.

The patient made an uneventful recovery and was discharged on July 7. Up to the time of this report she has experienced no further symptoms of abnormal bleeding, liver disease or thyrotoxicosis.

Discussion

Liver-function impairment with jaundice has been reported in conjunction with the use of thiourea compounds.[1-5] It is not the purpose of this paper to evaluate critically the significance of these reports. It seems that some patients, particularly those studied several years ago, may have been suffering from a coincidental attack of infectious or serum hepatitis. Certainly severe depression of liver function by propylthiouracil must be relatively rare in view of the paucity of articles dealing with this development, in spite of widespread use of the drug. The Council of Pharmacy and Chemistry of the American Medical Association does not even mention jaundice as a toxic effect of thiouracil.[4] Moore,[1] in his collected series, notes jaundice as one of several miscellaneous toxic reactions, all of which amount to about 2 per cent of all reactions to thiouracil. To our knowledge, no previous incident of isolated prothrombin deficiency without other signs of hepatic damage has been noted after the use of thiourea derivatives.

With the evidence at hand it is impossible to single out propylthiouracil as the only factor in the hypoprothrombinemia that developed in this case. However, the temporary nature of the phenomenon strongly suggests the type of reaction due to drug intoxication. The congenital idiopathic variety of hypothrombinemia seems to be excluded, since this form is usually persistent or recurrent and the prothrombin time remains elevated even though no actual bleeding may be present. This patient's prothrombin time returned to normal under treatment and remained normal.

Thyrotoxicosis itself has been thought by many to be associated with liver damage in a high percentage of cases.[6-9] The incidence and degree of hepatic damage reported have varied greatly in various reports. The highest percentage of definite pathologic change has been in series of autopsied

TABLE 1. *Effect of Various Types of Plasma and Serums on the Prothrombin Conversion Rate of the Patient's Plasma. Of interest are the increased activity of the serum after treatment and the marked effect of normal fresh serum as compared with that of plasma.*

	Control	Patient's	Patient's Plasma Normal Plasma (3:1)*	Patient's Plasma Normal Serum (3:1)	Patient's Plasma Patient's Serum (3:1)	Patient's Plasma Before Treatment Patient's Serum After Treatment†
Prothrombin time (seconds) ..	12	230	17	9	42	20

*Denotes the proportion of patient's plasma to added plasma or serum.
†Denotes patient's serum collected after treatment with fresh serum.

cases. As Means[10] points out, the elimination of other factors, such as glycogen depletion, which diminishes hepatic cellular resistance to noxious agents, is difficult in these severe cases in which death occurs from the complications of thyrotoxicosis. In his opinion the evidence for any specific hepatic disturbance due to overproduction of thyroid hormone is inconclusive at present.

In the case herein reported, disturbance of hepatic function in conjunction with the prothrombin depression was not detected. Therefore, if the prolonged prothrombin time was due to faulty production by the liver it seems to have occurred as an isolated phenomenon possibly similar to that seen with dicumarol or salicylate intoxication. It is unlikely that vitamin K deficiency or impaired absorption could have been responsible, since the food intake had been good, there was no evidence of other vitamin deficiency and parenterally administered vitamin K had no immediate effect on the prothrombin time, although a more delayed effect might have become apparent if other treatment had not been given. The possibility of some circulating substance's inhibiting the activity of prothrombin or its accelerator substances cannot be excluded altogether. It seems unlikely, however, since mixing the patient's plasma with normal plasma did not inhibit the prothrombin-conversion rate of the normal plasma beyond what would be expected from dilution alone.

Whatever the cause of the prolonged prothrombin time may have been, further studies indicated that the deficiency was primarily one of accelerator factor (or factors), which Seegers has designated as Ac-globulin. The data in Table 1 indicate that normal, thrombin-free serum (containing less than 10 per cent of normal plasma-prothrombin concentration) was capable of lowering the conversion time of the patient's plasma prothrombin to nine seconds. This indicates that normal serum, rich in Ac-globulin,[11] was capable of exerting a marked effect on the patient's prothrombin-conversion rate. This finding is similar to that previously reported by us in a case of idiopathic hypoprothrombinemia and in cases of dicumarol intoxication.[12] The effectiveness of normal serum in shortening the prothrombin time was also shown by the beneficial effect of intravenous serum (Fig. 1). Corollary data shown in Table 1 indicate that the patient's own serum lacked the potent effect of normal serum but that its effect was augmented after treatment of the patient with serum and whole blood.

Previous studies[12] have indicated that the most reliable method of quickly reducing the prolonged prothrombin time of such cases is the combined administration of fresh normal (thrombin-free) serum and fresh whole blood. According to our concept of the deficiency, such therapy provides accelerator substances with the serum and prothrombin with the whole blood. We have repeatedly found these measures more rapidly effective than any others, such as whole blood alone, intravenously injected vitamin K or vitamin K_1 oxide. It is again offered as a relatively effective, simple and safe means of reducing prolonged prothrombin time associated with deficiency of prothrombin and accelerator substances.

Summary

The case of a young girl receiving propylthiouracil therapy for thyrotoxicosis in whom severe hypoprothrombinemia developed is presented. No associated hepatic or hematologic disturbances were detected. The actual deficiency proved to be mainly one of accelerator globulin. Treatment with fresh human serum brought about a fall in prothrombin time and cessation of hemorrhage. The hemorrhagic tendency was kept under control with fresh serum and blood, and a subtotal thyroidectomy was successfully carried out.

The possible relation of propylthiouracil and thyrotoxicosis to the temporary hypoprothrombinemia is discussed.

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FIFTY YEARS OF MEDICAL PROGRESS

MEDICINE AS A SCIENCE: ROENTGENOLOGY

MERRILL C. SOSMAN, M.D.*

BOSTON

IN A recent article,[1] the present dean of American radiologists, Dr. Arthur Christie, quotes Arnold Toynbee[2] to the effect that retrogression is more natural than progression. He was speaking, however, of civilizations, not of men. Darwin[3] states that "progress is more general than retrogression" in the development of men and races. Robert Browning[4] even speaks of "Progress, man's distinctive mark alone." There is no "possible probable shadow of doubt" that medicine has progressed in the half-century just finished. True, it is less of an art and more of a science. True also, it is less of a profession and more of a vocation in many respects.

FIGURE 1. *Dr. Francis H. Williams at Work, Using an Induction Coil.*

His right hand controls the length of the spark gap, the amount of the condenser and the speed of the commutator, so that he can vary the light to suit his needs. The gas x-ray tube is in the box at the left. The revolving chair has a leather back through which the rays can easily pass. (Reproduced from Williams, F. H., The Roentgen Rays in Medicine and Surgery. Third edition. 757 pp. New York: Macmillan Co., 1903, by permission of the publisher.)

Medicine has become partly mechanized, but its modern efficiency in diagnosis and therapy cannot call forth any real regrets or any honest desire to return to the practices extant at the turn of the century. The ability to make a correct diagnosis in a given patient far exceeded the ability to treat the disease in the first four decades of this century. The development of roentgenologic diagnostic tests, to be summarized below, contributed largely to this state of affairs. In the past decade, therapy has made tremendous gains, as Fitz[5] points out. In fact, therapy with the new antibiotics is often started today in many illnesses before any attempt at differential diagnosis is made.

*Professor of radiology, Harvard Medical School; radiologist-in-chief, Peter Bent Brigham Hospital.

At the turn of the century, radiology was but four years of age, Roentgen having made his epochal announcement of "a new kind of ray" in January, 1896.[6, 7] By 1900, a considerable volume of literature had accumulated, but it was mostly reports of individual cases and experiments in the physical properties of the new ray or preposterous claims based on its use. X-rays were being used by physicists, engineers, photographers and by some charlatans, as well as a few honest physicians. In the latter group, Walter B. Cannon[8] had reported his studies of motility in the gastrointestinal tract, experiments begun as a medical student in May, 1897, during which he acquired burns on his hands, which were to trouble him for the rest of his life. Similarly, Francis H. Williams had reported his clinical observations on fluoroscopic examination of the heart and lungs,[9] and had even published a 532-page textbook on the subject.[10] These were but voices crying in the wilderness, and the physicians of those days turned to x-ray examination only in cases of fracture or of metallic foreign bodies. Progress was slow and uncertain early in the century. Tremendous growth and expansion came as the result of improved equipment, new methods of examination and the accumulation and exchange of knowledge by interested physicians. Progress can also be traced by the application of radiopaque substances used in radiology to secure contrast in the body cavities and hollow viscera. These were at first only inert materials either injected or ingested, but later the physiologic or functional excretory tests, such as cholecystography and urography, were developed. They all followed the same pattern — first the development of the test, then the application to clinical material with the resultant accumulation of data and finally the evaluation of results, which was always best done and most reliable when the work was carefully controlled.

EQUIPMENT

The early roentgen-ray equipment was inefficient, cumbersome and highly unreliable. Electrical power of sufficiently high voltage but of very low current was obtained from either induction coils (Fig. 1) or large static machines. Much of the radiologist's time and effort was spent in caring for his machine and his gas tubes. One had to be an artisan as well as an artist to get good "pictures" in those days.

The first of the ten major improvements in equipment was the invention of the "interrupterless transformer" by Clyde Snook.[11] Next was the hot cathode tube of W. D. Coolidge.[12] Then, for the

first time, the roentgenologist could calibrate his machines and duplicate his exposures. Precision replaced guesswork, and the new science was on a firm technical foundation. Double-emulsion films replaced the glass plates, as the third advance. Then came the Bucky–Potter grid,[13, 14] to eliminate the scattered rays. Valve tubes or kenetrons then supplanted the motors and rectifiers; next came the shockproofing of all exposed equipment. Now all x-ray machines are (or should be) shockproof. The rotating-anode tubes were seventh on the list, and the spot-film apparatus next. This had long been in use on the continent before it became popular here. Photofluorography was a direct outgrowth of the demand at the beginning of the second world war for a rapid yet accurate method of radiographing the chests of all draftees, volunteers and recruits primarily to detect pulmonary tuberculosis. This method was first developed by de Abreu,[16] of Brazil, using ordinary 35-mm. roll films. Largely due to Potter's efforts, the United States Army and draft boards adopted 4-by-5-inch cut film or a double (stereoscopic) 4-by-10-inch exposure. The Navy, maintaining its record for being different and independent, used the 35-mm. roll film. Both were very efficient. At the end of the war, the method had been markedly improved and was technically almost perfect and foolproof.[16] The value of this method in postwar mass chest surveys in detecting pulmonary tuberculosis can scarcely be overemphasized. It would rank with vaccination and inoculation as a preventive of the spread of disease if the unintelligent sections of our population could be required to co-operate in annual surveys. The Scandinavian countries are well ahead of us in this application of the principles of public health and preventive medicine.

The roentgen kymograph[17] and its modifications[18] have not added very much to the accuracy or value of our diagnoses. The tomograph, however (body-section roentgenography), has turned out to be a more helpful modification of standard equipment, as it produces clearer images of deep structures and sometimes uncovers important shadows that would otherwise be unrecognizable.[19]

Cinematography of the fluorescent screen has been accomplished by many workers and in many fields, but it is still of little value in differential diagnosis, due to the lack of detail inherent in the method. At present, its chief value is in demonstration of methods and teaching of principles to large audiences.

Plates, Films, Screens and Developers

At the turn of the century, and for two decades thereafter, the x-ray plate and its development were an important part of the practice of radiology. The heavy glass plate was at first developed individually in trays, usually by the radiologist himself. The development of x-ray films is today almost a lost art, often entrusted to the least competent person in the department, with the result that frequent artefacts confuse the unwary physician.

Films generally replaced the cumbersome, heavy plates about 1920, but met with resistance in many quarters, as they would belly out and be scratched during processing and would curl when dry. These difficulties were gradually overcome, and the advantages of films over plates soon became obvious to all. Mass production and streamlined methods were developed, and at present there are available automatic developing-fixing-washing-drying machines that take in the exposed but undeveloped film at one end and turn out the finished and dried film at the other end. All we need now is another machine to point out the pathologic process or to identify the disease, and radiologic diagnosis will be fully automatic!

The old glass plates had some compensations, in addition to being useful for cold frames or greenhouses. If the referring physician was not entirely satisfied with the quality of the plate (as Goethals notes in his tribute[20] to the late Percy Brown), the plate could easily be dropped—and that would end the discussion. Furthermore, they were more difficult to conceal or carry away. Handling a large number of plates, however, was quite a chore; I still remember taking, in one day, 150 chest plates* on half a dozen "pneumonia wards" with a portable machine and a team of six running corps men during the influenza epidemic of 1919!

Unfortunately, the films at first were made from a cellulose-nitrate base that was highly inflammable; the incomplete combustion of large stores of such films resulted in the terrible loss of life at the Cleveland Clinic in 1929. After this disaster a base of cellulose acetate was universally adopted — much less inflammable, but still dangerous if incompletely burned in close quarters, as the recent (1950) fire in Brompton Hospital, London, proved.†

Contrast Media and Methods of Examination

The pioneers in radiology at the turn of the century were making almost daily discoveries. Imagine, if you can, the thrill that came to MacIntyre,[21] of Glasgow, in June, 1896, when he was able to visualize, on his sixth attempt, a renal calculus! It required an exposure of twelve minutes and very careful development of the plates. Or that of Francis Williams, when he recognized early tuberculosis or pneumonia or pleural fluid under his fluoroscope. Chest examinations and many of the studies on fractures and foreign bodies in those days were made largely with the fluoroscope, as plates were difficult, uncertain and expensive. Williams'

*It is a strange anachronism that in many places roentgenograms of the chest are still referred to as "chest plates," even in Boston.

†This fire started in the basement in the department of pathology, directly adjacent to the thousands of x-ray films stored in open shelves. One pathologist lost his life, and a nurse at the far end of the building and on a different floor was overcome by the fumes and died from the effects — presumably carbon monoxide carried by the ventilating system.

work on the heart and lungs was far ahead of any other man's at that time, but his work on the stomach was mostly concerned with the size, shape and position of this organ. After Cannon's pioneering work,[9] it remained for Rieder,[22] in Germany, to adapt his ideas to clinical and morphologic studies, using a bismuth meal.*

By 1904, the beginning of accurate gastrointestinal examination was under way. On the Continent, this was known ever after as "Rieder's method," for it is usually not the discoverer of a new method, but the one who adapts it or popularizes it, who receives the credit. Soon the names of Holzknecht, Haudek, Cole and Carman came to the fore in gastrointestinal roentgenology. Gastric ulcers and cancers were recognized and differentiated by those men and their followers as early as 1910, but the characteristic signs of duodenal ulcer were not clarified until about 1914.[23] The extraordinary preponderance of duodenal ulcers over gastric ulcers was not appreciated for another decade, but it was by the roentgen method that this common ailment of worried or unhappy adults was finally established as a clinical entity. This was all the more remarkable, as the autopsy figures up to that time indicated a preponderance of gastric ulcers over the duodenal or postpyloric ulcer. This also seems to prove the truth of one of my favorite axioms: "We see only what we look for."

From 1920 on, the accuracy of roentgen diagnoses of morphologic changes in the gastrointestinal tract steadily improved, helped immeasurably in this country by Carman's excellent textbook[24] and aided by the constant improvement in equipment and materials as noted above, until at the present time an expert radiologist can demonstrate about 85 per cent of significant lesions and identify those demonstrated in 90 per cent.

The gall bladder and its diseases, on the other hand, remained largely inaccessible to the roentgen method, other than the 20 per cent of "positive" gallstones and the rather questionable "indirect" signs of reflex changes in gastric activity, until Graham,[25] in 1924, put the keystone of inductive reasoning in the arch of knowledge concerning phenolphthalein,† and, with the help of Mallinckrodt's chemists, announced the cholecystographic technic that bears his name. This method was promptly tested and standardized by many workers. This was the first of the combined functional and morphologic tests in roentgenology, and has become one of the most accurate and reliable of all roentgen examinations. In good hands, and with good roentgenographic technic, the accuracy should be 98.5 per cent or better. I know of no other test in medicine that approaches this in accuracy.

The lungs were, of course, one of the first of our anatomic structures to fall under roentgen-ray scrutiny; they were peculiarly adapted to the method because of the natural contrast between the air-filled normal lungs and the pathologic states of infiltration, destruction and consolidation. Abnormal conditions could be demonstrated easily, but it took years, and the accumulation of considerable experience, before an accurate differential diagnosis could be made in many cases. Even now, although we can demonstrate significant lesions in the lungs in a high percentage of cases, it is often difficult or impossible to identify them etiologically or histologically. It is amusing to record that progress in this field not only was slow and against considerable resistance from the highly trained stethoscopists but also occasionally led into blind alleys or even false pathways. In 1907 Cole, of New York, after presenting a paper on the roentgen detection of early pulmonary tuberculosis in the absence of physical signs and symptoms, was censured by the officers of the society for presenting such absurd claims and preposterous statements.[26]

The influenza epidemics of 1918 and 1919 and the regrettable incidence of tuberculosis in members of the armed forces of the first world war were great stimuli to the development of pulmonary roentgenology. In addition, large numbers of physicians were given basic training in the military schools of roentgenology established at Camp Greenleaf and continued at the Army Medical School in Washington. Most of these men remained in this specialty on their return to civilian life. Furthermore, many other physicians first learned the advantages of roentgenology while serving in the armed forces, subsequently demanding this service in their civilian hospitals and practice. The shortage of equipment, particularly of fluorescent screens, formerly imported from France and Germany, also forced our manufacturers to meet the demand, with consequent improvement in our own products. However, one of the false leads that brought the roentgen method temporarily into disrepute was a sequel of the influenza epidemic. This was the marked increase in the number of diagnoses of "peribronchial tuberculosis" on roentgen examination, now known to have been an organizing interstitial pneumonitis, which was an all-too-common sequel of influenza in those years. This particular diagnosis of "peribronchial tuberculosis" has gone into the discard, along with "visceroptosis" (Glenard's disease) and the "incompetent ileocecal valve," which also had their strong supporters among the radiologists.

The one important thing that was missing in the early years of chest roentgenology was an accurate control study of diagnoses made by any method. Most of the diseases were chronic; many were self-

*Rieder at first used bismuth subnitrate, then the subcarbonate and finally the oxychloride. Cases of bismuth poisoning were not uncommon, because of soluble salts of bismuth present as impurities. Barium sulfate was introduced about 1910, and was in general use by 1920. It was not only safer, being completely insoluble and more easily purified, but also much cheaper, costing less than one tenth the price of bismuth salts.

†Graham's idea of adding a roentgen-opaque iodine radical to tetrachlorphenolphthalein was the final step in the work done by many men, among them Abel, Geraghty, Rowntree and many others. The same idea had occurred to other men, but it had been dismissed as impossible or impractical. Graham had the courage to try it, and succeeded.

limiting, and about the only conditions that could be promptly verified were pleural effusions and empyemas. Gastric washings and sputum cultures for the tubercle bacillus were not available, and even the bravest of surgeons dared not invade the thorax, except to drain a lung abscess or an empyema. By contrast, a roentgen diagnosis of cancer of the stomach or colon or of gallstones or urinary calculus could promptly be verified or disproved by operation. Carman's reputation and the value of his book were greatly enhanced by his painstaking control of his roentgen findings, as he worked in a predominantly surgical clinic with a high percentage of exploratory operations.

The other important diseases of the lungs slowly came into focus, such as silicosis, foreign bodies in the bronchi and bronchiectasis, helped respectively by the work of Pancoast and Pendergrass, Chevalier Jackson and Manges and Forrestier and Sicard. The latter pair, by 1922, had injected their favorite lipiodol into every available opening and into every hollow or potentially hollow space. Cancer of the lung, however, was slow to be recognized, and there is still plenty of room for argument about whether it is really on the increase at present or is simply recognized more frequently by means of better roentgen examinations, bronchoscopy and exploratory operations.

The heart was also one of the first organs to be studied by the new roentgen method. Williams made repeated observations on the size, shape, activity and mobility of the heart under the fluoroscope and published many of his observations and deductions in the medical journals of the times and in his book.[10] Willliams was helped by his brother-in-law, Rollins (a dentist with a degree from M.I.T.), chiefly along technical lines. Together they invented and described the "See-Hear," a combination of fluoroscopic screen and stethoscope whereby they could simultaneously observe the heart in action and hear its sounds. Many other ingenious modifications of existing apparatus are described in his book, the later editions of which even included chapters on roentgen therapy. Rollins also published a book, "Notes on X-Light," concerned chiefly with technical apparatus but far ahead of its time in most of its observations and designs.[27]

The early work on cardiac roentgenology was limited by the static concept of disease then prevalent; much of it was devoted to the discovery and identification of aneurysms of the aorta. In the field of cardiac roentgenology, the French roentgenologists (such as Vaquez and Bordet[28]) were probably ahead of their German and Austrian colleagues, but the latter were for years the leaders in all other branches of the specialty. The French also led, naturally, in radium therapy. The medical centers of Germany and Austria were the Meccas for all earnest students of the specialty,[29] partly because of the high percentage of autopsies that confirmed or disproved their observations and deductions and partly because of the physicians' boldness and the patients' passivity in investigation. After the first world war, leadership passed to Sweden, England and the United States. At present, Sweden probably leads in general radiology, with Great Britain showing much progress in radiotherapy. Nearly every civilized country has made some outstanding contributions to roentgenologic diagnosis: Moniz,[30] of Portugal, to cerebral angiography; de Abreu,[15] of Brazil, to mass chest surveys; Forssell[31] and Akerlund,[32] of Sweden, to detailed mucosal studies in the gastrointestinal tract; Castellanos,[33] of Cuba, to angiocardiography; and, not the least of them, Dandy,[34] of Baltimore, to ventriculography and Graham[35] and his colleagues, of St. Louis, to cholecystography.[36]

Therapy

It was a matter of only a few weeks after the announcement of the "new kind of ray" that its

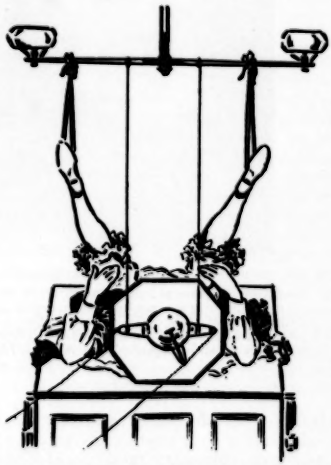

Figure 2. *Early Intravaginal X-ray Therapy, Using a Large Metal Perineal Shield and a Vaginal Cone Through the Shield. (Reproduced from Allen, C. W.* Radiotherapy and Phototherapy, Including Radium and High-Frequency Currents. *618 pp. New York: Lea Bros. and Co., 1904, by permission of the publisher.)*

effects upon the human skin were noted. In our own country, E. H. Grubbe, of Chicago, a manufacturer of Crookes tubes, was suffering from "dermatitis" of his hands when the announcement was received. A deliberate exposure to x-rays for therapeutic purposes was given by Grubbe at the request of a physician on January 29, 1896 — probably the first x-ray therapy on record.[36] "Sunburn"

and "eczema" were reported on the hands of workers with x-rays in April and May of 1896, probably because they tested the "hardness" of their gas tubes by fluoroscoping their own hands! Elihu Thomson reported March 4, 1896,[37] that he had exposed the little finger of his hand, with a resultant blister. He emphasized the fact that only the part actually exposed was affected; he also noted both the latent period and the cumulative effect.

Therapeutically, the first attack was on bacteria and bacterial diseases, but with disappointing results, although the literature of the early nineteen hundreds reveals numerous articles reporting the good effects of x-ray treatments (combined with bed rest) upon pulmonary tuberculosis! Epilation was noted in April, 1896, and the first deliberate attempt to treat a neoplasm was that given to a hairy nevus by Leopold Freund, of Vienna, in which he made a logical deduction and planned a trial of the new rays. He gave treatments of two hours per day, one area of the large nevus receiving forty-two hours of irradiation! The only measure of intensity was "that which permitted a hand to be photographed in one minute." Epilation resulted on the seventh day. The ulceration that followed later required several excisions, but five years later only a small portion of the original nevus remained.[38]

By 1902, uterine fibroids, the ovaries and cancer of the uterine cervix were being treated by roentgen rays; even intravaginal cone therapy was being used, the patient's legs being suspended from the gas chandelier (Fig. 2). In 1903, Pusey[39] and Senn[40] reported on the x-ray treatment of leukemia; a short time later, many authors reported good results in the treatment of Hodgkin's disease and "lymphadenoma," although the exact classification of many of the tumors was doubtful (Fig. 3). Then came carcinoma of the breast, sarcomas of bone and soft tissues and goiters of all kinds. Even epilepsy, diabetes, angina, varicose veins, trachoma and pulmonary tuberculosis were reported as "improved" under x-ray treatment.

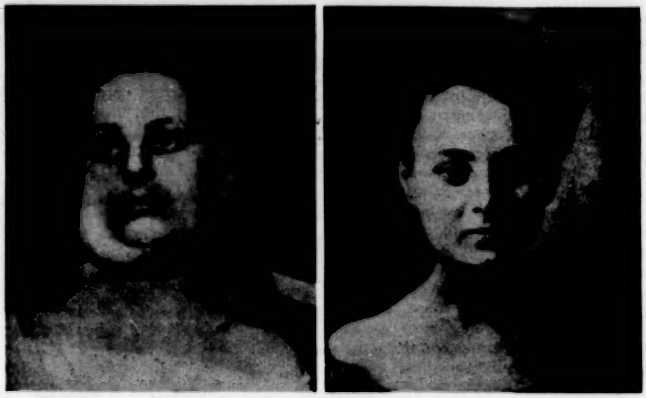

FIGURE 3. *Early Result of X-ray Therapy in Malignant Lymphoma (1902).*
Patient 12 years of age; treatment begun in May, 1902; exposures "once or twice a week during ten months." "She was weak and listless at the beginning of the treatment, but became bright and active after the lapse of three or four weeks." Two operations, microscopical diagnosis first "lymphosarcoma," second biopsy "round-celled sarcoma." (Reproduced from Williams, F. H.: The Roentgen Rays and Medicine and Surgery. *Third edition. 757 pp. New York: Macmillan Co., 1903, by permission of the publisher.)*

The early methods of measurement, or, rather, estimation of doses, were by rule of thumb only and were based on trial-and-error technics. The erythema was the standard reaction, and time was at first the only factor. Later, the distance of the tube from the skin was found to be important, and in 1906 Pfahler[41] advocated the use of a leather filter as most nearly approximating a thick layer of human skin. In the early days, the metal filter was grounded to shield the patient from the effects of the electrical field, which was thought by some to be causing the "dermatitis." Unfortunately, the accurate observations of Elihu Thomson, Rollins and most physicists were published in electrical or engineering journals and were not read by the

physicians using the rays for clinical purposes. It took some time to co-ordinate the efforts of engineers, physicists, manufacturers and clinicians. Accurate measurement of doses was not possible until the advent of the Coolidge tube; even then the standard was the number of milliampere-minutes per treatment. In 1904, Perthes[42] made the first depth dose measurements, proving the value of filtration; this was further developed by Dessauer,[43] who proved selective absorption of the rays. The ionizing effect of x-rays was noted by Roentgen in his original experiments, but there were no instruments to measure it. These were developed eventually by Villard, Duane, Friedrich and others. Duane[44] promulgated his R unit in 1914, but many workers had conceived other units; it was not until the International Congress in 1928 that an international unit, the "r" (for Roentgen) unit, was adopted by all countries.[45]

The Germans Seitz and Wintz[46] in the meantime had developed and popularized the "massive dose technic" of delivering the greatest possible amount of ionizing rays to the tumor in the shortest possible time — in striking contrast to the French method, advocated particularly by Coutard,[47] of small doses daily (or twice a day) to the tumor, protracted over a long period of time, with observation of both patient and tumor during the treatments. It was quite a battle: the German blitz technic of "Kill the tumor" (never mind the patient) versus the French technic of "Treat the patient, who is the host, and let him help you get rid of the tumor." At the present time, the fractionated or French technic is followed by the majority of radiologists; it is in reality a partial return to the earliest days of roentgen therapy, when small daily doses were given by necessity and the effect carefully watched, but without the knowledge of what was being given in terms of quality and quantity and without knowledge of what to expect.

As therapy equipment improved, the technics of measuring and administering radiation improved, with correspondingly better end results. Higher voltages and heavier filters gave better depth doses, with less damage to the normal skin and tissues overlying the tumor. The idea of cross-firing a deep tumor through several portals of entry was developed by Dessauer.[43] This was quite necessary in the use of 200-kilovolt therapy but is now unnecessary with supervoltage machines. The first isodose curves were developed by Friedrich and Glasser[48] and are now an integral part of all deep-therapy calculations. The instruments for measuring the doses while they are being given, the methods of testing tumors for radiosensitivity and the calculations of doses necessary to kill the tumor while not irreparably injuring the surrounding normal tissues have all improved greatly. The advent of supervoltage machines — first 400 kv., then 800, 1,000 and 2,000 kilovolts and now the cyclotron, betatron and linear accelerator, as well as radioactive isotopes — has radically changed many of our concepts and has made a highly specialized field out of what was once a subordinate part of radiology. The full-time radiotherapist of the future will probably be entirely separate from the general or diagnostic radiologist, at least in the larger centers.[49] The danger is that a group of incurable optimists will be formed who believe that twice the dose will kill twice as many tumors — a return in principle to the disastrous days of the German blitz technics. In some places, notably England, the radiophysicist has already been elevated to a much higher position than he deserves, and treatments to patients are determined by the slide rule, the adding machine and the isodose curves, rather than by clinical judgment. Inasmuch as a high percentage of radiotherapy is purely palliative from the first day the patient is seen, such heroic attempts to cure the incurable are to be viewed with healthy skepticism rather than enthusiasm.

Protection

The lack of protection against the injurious effects of the new rays must have been due either to ignorance or indifference, for plenty of warnings appeared, both spoken and written, within a few months after Roentgen's announcement. Many of these warnings, unfortunately, were published in journals devoted to electricity or to physics and therefore were not seen or heeded by physicians. The whole history of protection records a series of pendulum-like swings. As new examples of irradiation damage became known protection was increased, but as there was no sensation from overexposure to the rays, neglect of precautions inevitably followed until another tragedy was made public. The early efforts toward shielding were made on the operator's person, but as this was cumbersome and inefficient the protection was shifted to the tube. Lead-glass windows were available and in use as early as 1900, but by this time Codman[50] was able to collect 170 cases of injury due to roentgen rays, about half of them of serious degree. As noted above, there was a period of argument concerning whether the cutaneous burns were due to the electrostatic field or to the rays themselves, and there was further argument about whether the static machine produced less harmful effects than the induction coils. Gradually it was learned that the x-rays were really the deleterious agents and that harm could be prevented either by keeping at a safe distance from the rays or by interposing metal shields between the source of the rays and the operator. Several instances of acute deaths from overexposure were recorded at the turn of the century, and many other cases of severe roentgen sickness (but with recovery) are also known. Here in New England, Joseph Godsoe, Walter Dodd's assistant, was an example. Dr.

Warren wanted a complete set of normal plates for reference; one evening Godsoe was the willing subject of a long series of exposures, of an unknown total but enough to put him to bed in a state of collapse for several days! By contrast, Francis Williams, one of the earliest pioneers, and one who did more fluoroscopy than any of his colleagues, always protected himself adequately; at his death (at 84) he was free from any evidence of radiation injury. An even more striking contrast was seen in two of Dodd's pupils who started work at about the same time and did about the same amount and variety of work. One was always careful not to expose his hands to the direct beam of x-rays in fluoroscoping his patients; as a result, his hands today, at the age of 74, bear no evidence of radiation injury. The other one always used his bare hands to palpate the patient's abdomen, believing that he could learn more by feeling while seeing, and deliberately disregarded his own safety. He died in 1933, at the age of 58, from radiation-induced carcinoma of the skin of his hands. The lives, works and sufferings of many of the early American pioneers in radiology are well told in the late Percy Brown's memorable book "American Martyrs to Science through Roentgen Rays."[81]

With the change to the higher-powered transformers and the larger output of Coolidge tubes, adequate protection became a necessity in the second decade of the century. Committees on protection and safety were formed in the radiologic societies, and the Bureau of Standards was asked to draw up rules and regulations for the protection of workers in roentgenologic fields. There was no police power to enforce such rules, but they were accepted and followed everywhere — at least in spirit if not to the letter. It always was and still is possible to receive serious injury from the daily use of the roentgen rays or radium, but for the past quarter-century everyone working with these agents has known how to avoid that injury. Individual carelessness or willful disregard of rules cannot as yet be prevented.

In the early years of the specialty — in fact, the first quarter of this century — the manufacturers of roentgen equipment seemed to neglect the factor of safety. The protections recommended by the British Roentgen Society after the first world war were approved by a safety committee at the second international congress of radiology in Stockholm in 1928, but only the British equipment came up to specifications at that meeting. Three years later, at the next congress, there was a marked improvement in regard to safety features incorporated in equipment.

The atom bomb, and all the publicity concerning radiation effects, gave a great impetus to methods and plans for protection. At the present time, the pendulum has swung almost too far in the other direction. Insurance companies, building inspectors, health departments and politicians are all becoming guardians of the public health, and many absurd restrictions are being suggested. The furore has at least made everyone conscious of the danger and has resulted in various forms of monitoring schemes and devices. The danger, of course, increases with the increase in voltage, and the greatest hazards today concern the cyclotrons, betatrons and other multi-million-volt installations. The danger is still great, however, in the daily handling of radium or the radioactive isotopes, as well as in the daily use of fluoroscopy. It is all the more deadly because the lethal effects cannot be perceived by the person suffering from them. With hundreds or thousands of investigators now using the radioactive isotopes, there will almost certainly be numerous cases of irradiation damage that may take months or even years to show up.

The development of radiobiology and the use of the roentgen rays in industry both deserve more than mention, but there is no space for it in this paper. The radiobiologist and the radiophysicist have contributed particularly to the progress of therapy. The widespread use of x-ray examination of castings and airplane parts in the late war was a new development and helped in improving equipment, particularly in high-voltage lines, and in standardization of procedures. Many of the discoveries and inventions used in industry have been adapted to clinical use.

Journals and Books

At the turn of the century there was only one American journal devoted to roentgenology, the *American X-ray Journal*, published by Dr. Hebar Roberts of St. Louis (Fig. 4). This ran for only a few years, and was succeeded by the *Transactions of the American Roentgen Ray Society*. These *Transactions* were expanded to the *American Quarterly of Roentgenology* in 1906, edited by Hickey, of Ann Arbor. This in turn was changed to a monthly journal in 1914, the *American Journal of Roentgenology*, now one of the best radiologic journals in the world. Since 1923, it has been known as the *American Journal of Roentgenology and Radium Therapy*, now in its sixty-fifth volume.

The other modern American journal, *Radiology*, was originally sponsored by the Western Roentgen Society as the *Journal of Roentgenology*. The new journal, *Radiology*, was started in September, 1923, and has been in continuous publication since; it is now in its fifty-sixth volume. These two journals together are probably the best and most widely read source of radiologic information in the world today.

The British were the first to organize a society and sponsor a journal. Even before Roentgen read his third (and last) communication,[82] the "Skiagraphic Society" was founded in London and its journal, the *Archives of Clinical Skiagraphy*, inaugurated. The skiagraphic journal's name was

changed to the *Archives of the Roentgen Ray* until 1917, when it became the *British Journal of Radiology* by fusion with the *Journal of the Roentgen Society* (established in 1904). This journal devoted considerable space to physics, electrology and the technical work of radiography, so that only recently a new journal, the *Journal of the Faculty of Radiologists*, has been launched, devoted primarily to clinical radiology.

The Germans led the world for years in the excellence of their roentgenologic journals and particularly in the clarity of their illustrations. The *Fortschritte auf dem Gebiete der Roentgenstrahlen* was begun in 1897 under the guidance of Albers-Schönberg, and was widely read and quoted everywhere until the rising power of Hitler put the curse on it, as it did on so many scientific and literary endeavors. This excellent journal has not yet recovered its prestige, so far as I know. *Strahlentherapie* was founded in 1912 and was the Bible of radiotherapy and radiophysics for many years. The third journal, *Roentgen-Praxis*, gave competition to the others and afforded another outlet for the voluminous literature of the first country to measure a man's eminence by the number (not the worth) of the articles he had fathered. *Roentgen-Praxis* and the *Fortschritte* have recently (1949) been combined into a single journal. The five Scandinavian countries formed an association in 1920 and under the leadership of the late great Gösta Forssell founded the *Acta Radiologica*, now one of the best radiologic journals. Forssell did more for radiology in Europe than any other man to date, and radiologists all over the world mourn his recent (1950) death.

The French were late in founding a society (1907) and a journal (1909); the latter has never reached the eminence of the American, German and Swedish journals — perhaps because it was also the organ for electrology and electrotherapy.[53]

Books

The early books of Francis Williams and Rollins have already been mentioned. One of the earliest (1896) was Morton's[54] *The X-ray, or Photography of the Invisible*, containing some excellent illustrations. Dr. Carl Beck,[55] a surgeon in New York, published two books, one (in German) in 1902 on diagnosis and therapy, particularly as related to surgery. Pusey and Caldwell's book on the practical application of the x-rays[39] was published in 1903, and Rollins' *Notes on X-Light* in 1904. Germany was again the source of many atlases and supplements to the *Fortschritte*, as well as of individual monographs and textbooks that were widely read, some of them being translated into other languages.

Since those early days, literally thousands of books on roentgenology and radiotherapy have seen the light of day, in all countries of the world. At this midcentury pause, the literature on artificial radioactivity alone would keep a good-sized team of men busy reading twelve hours a day to keep up with it.

Present Status of Radiology

Radiology is today the most widely used consultative specialty in medicine, and is of great value to all the specialties, even including psychiatry.

Figure 4. *Cover of the First Issue of Hebar Roberts'* American X-ray Journal.

Dr. Percy Brown says: "The allegorical figure of Science is seen to be irradiating the globe with the emanations of a double-focus Crookes' tube energized from a Knott high-frequency coil at the lower right-hand corner. In front of the coil is supported another tube, evidently in reserve. No detail is omitted, even the corona along one of the cathodal leads being suggested. The border is appropriately ornamented with multiple Lamps of Knowledge." (Reproduced from Brown,[51] *by permission of the publisher.)*

The work of all x-ray departments has at least quadrupled in the thirty years of my own experience, and it has also increased in accuracy and reliability as well as in complexity. It has reached a plane of availability and usefulness hardly dreamed of by the pioneers in the field. As Forssell wrote twenty-five years ago,[56] "Radiology has progressed from being simply a method of examination to the present status of a full-grown independent and extensive science." The accuracy and reliability of roentgen diagnoses have been detailed in a recent Shattuck lecture,[57] and will not be summarized here.

Carman, in 1920, used only three shades of opinion: "possible," "probable" and "definite." As a rule it is easier to demonstrate an abnormality by roentgen examination than it is to identify it etiologically or histologically, particularly in the lungs.

Many of our patients, unfortunately, think that the x-ray examination is infallible, and that the fluoroscope or the film will reveal the cause of all their troubles. Some roentgenologists even foster this impression of infallibility, particularly those of positive natures. Dogmatic statements or conclusions may often be made when the evidence justifies them, but it usually requires a man of wide experience and sound judgment to evaluate properly all the evidence in a difficult or complicated case. Such dogmatism is more prevalent where clinical control is lacking. At the other extreme, equal harm is done by the timid souls who are afraid to commit themselves even when the evidence is valid and conclusive. The practice of a specialty does not change the personality of the physician who enters it. True, most successful surgeons are decided extroverts, and the pathologists as a class tend to be introverts, with the internists in between, but we have all three types in radiology.

The tremendous clinical help that is afforded all branches of medicine and surgery by good radiologic practice has led to several abuses. Chief among them is the dependence of many physicians upon the radiologist for a diagnosis, to the extent that the patient may be sent for x-ray examination without having had either an adequate history or physical examination. This leads to unnecessary work and extra expense, reflected in the increasing costs of medical care. This may be more prevalent in general practice, but even in the better hospitals many unnecessary radiologic examinations are done. This does not apply, of course, to routine screening procedures such as photofluorography of the chest, but it does apply particularly to the time-consuming and difficult gastrointestinal examinations for every form of abdominal distress. We must admit, however, that every now and then an unexpected and sometimes important lesion is discovered, so that the practice is not entirely without justification. One of my colleagues made it his regular practice to do a complete roentgen survey of patients referred to him by certain physicians, knowing that they were depending on him to make the diagnosis, if possible, for them. He would first make films of the abdomen for liver, spleen, kidneys, pelvic organs, spine and pelvis and then cholecystograms, barium-enema and upper-gastrointestinal studies; fluoroscopy of the heart and lungs followed the gastrointestinal series. He made a thorough physical examination of the patient by the roentgen method and established an enviable reputation for helping colleagues who were either too busy or too unsure of themselves to do their share. Perhaps I am wrong in calling this an abuse, and perhaps such routine examinations will become standard procedure, but if it does the cost of medical care will mount still higher and the complaints from the public will become louder.

Another major difficulty in the specialty of radiology that has developed in the past half-century is the economic one. As in the development of nearly all diagnostic tests, the early efforts at radiologic diagnosis and therapy were supported by hospitals or other institutions, or by private physicians who considered it merely a part of their physical examination. I am unable to ascertain when the status changed from an experimental to a routine one, and when the payment of fees for roentgen examination was instituted. This probably occurred in the first decade of this century. The equipment then was relatively simple and the x-ray tubes inexpensive, so that the costs were low. It soon became apparent, probably at the end of the second decade, that the hospital departments of roentgenology not only could be made self-supporting by means of fees but also could be depended upon to produce revenue in excess of expenses. This tendency was exaggerated as hospital expenses mounted and as the work (and income) in the x-ray departments increased. At the present time nearly all well conducted radiologic departments (except in charity or municipal institutions) finish the year with a definite excess of income over expenses, even including all the hidden expenses. Some of the largest ones are definitely budgeted to produce a considerable revenue each year, which is used to help in defraying the costs of other non-revenue-producing activities. This is in reality an economic noose around the neck of the specialty, as many hospital directors would like to hire a young radiologist at a moderate salary (no larger than their own) and keep the profit from the department for general expenses. The top fees, such as are charged in the best departments, are levied on the patients in second-rate departments, and the patients are unknowingly forced to contribute thereby to the support of the hospital's general activities. Undoubtedly many patients, and some radiologists, are thus exploited. On the other hand, there are probably just as many examples where the radiologist exploits the hospital (and of course the patients) by inadequate service, particularly in time and personal attention, in relation to the income received.

The remedy? First, more and better radiologists, so that all hospitals may be adequately covered, and secondly, a revision of charges and elimination of waste so that each department in the hospital becomes self-supporting. The endowment funds and grants can then be used for the indigent, or for research and development as specified. No clinical department should be considered as part of a supermarket, to make up the losses in one branch by excess profits from another activity. Time,

and the development of medicine as a whole, will probably settle the problem for us before the conflicting ideas and plans can be adjudicated.

A third important phase of radiology today is the activity along public-health lines, particularly in chest surveys. Ever since the development of satisfactory methods for mass chest screening during World War II, the idea has been spreading of applying the principle to large segments of our population, with the goal of discovering disease in the incipient and curable stages. This principle is applicable particularly to pulmonary tuberculosis, and to date about a dozen of our large urban populations have participated in such community public-health efforts. The dividends have been real and tangible, even though the surveys have not been as complete or all-inclusive as could be desired. Pulmonary tuberculosis could be wiped out if compulsory co-operation in annual mass chest surveys could be secured, as has been achieved in the Scandinavian countries. Similar dividends are not to be expected from survey procedures in gastrointestinal roentgenography, but pilot experiments are underway, in several institutions, that should clarify the magnitude of the problem and the frequency of unsuspected but curable lesions disclosed by routine methods. Mass chest surveys may be of considerable value in the discovery of unrecognized cases of heart disease.[58]

Avenues for Future Progress

The radiologist, who is permitted insight where ordinary vision is impossible, might also be expected to indulge in prophecy. But the future of radiology, as well as that of medicine in general, is in the hands of the gods, or, as some believe, in the hands of the politicians. However, several avenues of progress are now being developed, and still others are discernible as either possible or desirable. Certainly one general aim is both desirable and possible: more and better radiologic service for every individual and every community. This is not to be a substitute for other methods of examination noted above, but a carefully planned, co-ordinated and economically sound system of distributing the best available service where it is most needed and where it will do the most good. Perhaps centralized or regional institutes subsidized by the smaller communities, possibly aided by state or Federal funds and including pathological, bacteriologic and clinical laboratories as well as radiological services, may be the answer. This theme has already been developed and advocated by the Kellogg Foundation. On a higher level, specialized hospitals or institutes might be advocated, such as the cancer institutes of Sweden or London, where the best possible treatment of patients with cancer could proceed hand in hand with research. Certainly the present duplication of equipment and effort in many smaller centers could be bettered by co-operation and co-ordination. Similarly, in the training of young men to enter the specialty, the results could be improved by co-operation and consolidation. One fact still remains unchanged in this field: The selection of the candidate to receive the training is probably more important than the curriculum, the instructor or the institution.

One predictable change is on the horizon: the separation of the field of radiology into two separate specialties, one of diagnosis and one of therapy. Ideally, the training of the candidate should be quite different in the two fields — in diagnosis, based on anatomy, pathology, physiology and the whole field of clinical medicine and the specialties; in radiotherapy, on special training in tumor pathology, a good foundation in surgery and advanced work in radiobiology and radiophysics, in addition to training and experience in clinical therapy.[59] The field of diagnostic radiology alone is so comprehensive and so varied that subspecialties have been developed in the larger centers through concentrated effort and study in special anatomic fields such as the brain, heart and gastrointestinal tract or in the field of pediatrics. The results of such concentrated studies have added a great deal to our general knowledge and diagnostic acumen. To men like Dyke, Pendergrass, Robb, Steinberg, Sussman, Golden, Templeton, Rigler, Caffey and Neuhauser, to cite only a few, the radiologists are deeply indebted for authoritative works in their special fields. The future development of diagnostic methods and greater accuracy may well lie in the hands of such specialists.[59] Under present conditions, however, it will still be necessary to train a man in all fields to take care of the work in the community hospitals.

In the field of radioactive isotopes, the radiologist of the future should play a dual role. He should be on the safety or protection committee because of his knowledge of the inherent dangers and his experience in estimating and monitoring the dangerous areas. In cases where radioactive isotopes are used for therapeutic purposes, he should be called upon to assist in calculating the proper dosage and in arranging for the proper disposal of radioactive wastes. Records of such treatments should be filed in his department with other records of therapeutic irradiation. It will be necessary to include training in radioactive technics in the curricula of the training centers in radiology.

Several specific avenues of desirable improvement are already in view along technical lines. One of these is the amplification of the fluoroscopic image to the brightness and detail afforded by a good film.[10, 35, 60, 61] This has already been achieved by Dr. Edward Chamberlain of Temple Medical School, Dr. Morgan of Johns Hopkins and Dr. Paul Hodges and his team at the University of Chicago. Another note of progress can be made in this connection. Most of the early improvements in equipment and

discoveries of methods were contributed to the specialty by others than radiologists, but these three men are all physician-radiologists and all have other important contributions to their credit. It is both stimulating and comforting to see intellectual teams competing for scientific leadership at this level. The methods of amplification of the fluoroscopic image are complicated and highly technical at present, but it may not be long before electron tubes are available for clinical use.

A third possible improvement that would add to the usefulness and value of radiologic diagnosis would be a method of rapid development, fixation or clearing and drying of the photographic image so that the result could be reported almost immediately to the physician or clinic. If the Land camera technic (in which a completed photographic print is available within a minute after the exposure is made) could be adapted to x-ray films, it would speed up our work considerably. Patients could be seen in the clinic and radiographed there, and the report might be available before the patient leaves, thus facilitating diagnosis, decision and disposition of the case.

A method of visualizing the structure of the liver and pancreas without danger to the patient is highly desirable. Thorotrast, at present used to visualize the liver and spleen, is radioactive and dangerous to the patient. The liver and pancreas are the only remaining organs that cannot be studied satisfactorily by the roentgen method.

Conclusion

The progress in radiology in the past half-century has kept pace with the phenomenal development of science and medicine. Radiology has, in fact, contributed largely to the improvement of medicine, both in diagnosis and in therapy. Roentgen's discoveries preceded other adventures in radiant energy, of both peaceful and sinister import; let us hope that their beneficial use may continue to exceed the destruction of which they are capable. It seems at present that the x-ray is here to stay.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 37151

PRESENTATION OF CASE

First admission. A fifty-year-old woman entered the hospital complaining of vomiting.

The patient had had severe emotional difficulties all her life, which were currently centered about excessive dependence of her aged parents, strong religious preoccupations and conflicts, a late marriage with poor marital adjustment and a failure to have children. However, until the age of 46 her general health had been good except for extreme nervousness and painful blanching of the hands and feet on exposure to cold. Three or four years before admission, coincident with the menopause, the patient noted the insidious onset of postprandial discomfort, gaseous eructations and a feeling that food was remaining in the stomach for some time before passing. One year before admission she began to have steady, severe epigastric pain, which usually came on after eating and was relieved by induced vomiting or by the passage of time. Nine months before admission she began to vomit spontaneously any food eaten unless it was taken very slowly in small amounts and in soft form. The vomitus contained much bile but no blood. X-ray studies of the upper gastrointestinal tract, colon and gall bladder at this time at another hospital showed dilation of the third and fourth portions of the duodenum. Various oral medications were tried without relief, and in the months immediately preceding admission the patient became too weak and dizzy to work. She had lost 40 pounds, going from 130 to 90 pounds in weight, in the two years preceding admission.

Physical examination revealed a pale, emaciated woman with dry atrophic skin in which no focal lesions were noted. When exposed to cold, the hands first reddened and then became white and painful. The examination was otherwise normal.

FIGURE 1. *Narrowed Lower Esophagus with Ulceration and Hiatus Hernia.*

The blood pressure was 120 systolic, 75 diastolic.

Urine and blood examinations were within normal limits. The nonprotein nitrogen was 18 mg. and the total protein 6.1 gm. per 100 cc. Gastric analysis yielded no free acid, either before or after administration of histamine. X-ray films of the chest showed only emphysema. A gastrointestinal series demonstrated retained fluid in the esophagus at the beginning of the examination and a hiatus hernia 7 cm. long. Just above this in the esophagus was

an ulcer crater 3 mm. deep and 6 mm. in diameter around which the esophagus was stiff and narrowed (Fig. 1). The stomach was atonic and contained much secretion; however, no filling defect was found. The duodenal bulb and third portion of the duodenum were likewise atonic and dilated. Barium flowed into the jejunum with some difficulty, and serial films showed retention of material in the stomach and third portion of the duodenum. Esophagoscopy revealed a severe hemorrhagic esophagitis, and a biopsy was reported as acute and chronic inflammation, severe.

Although there were several episodes of vomiting during the hospital course, the patient was able to take a soft diet and was discharged improved on the twenty-first hospital day, weighing 94 pounds.

Final admission (eleven months later). During the next seven months the patient had three brief hospital admissions for esophageal bougienage, each followed by slight, transient subjective improvement. A gastrointestinal series made at the same time showed marked decrease in the size of the esophageal ulcer, although the narrowing and stiffening remained. The atony and dilatation of the upper gastrointestinal tract now involved the proximal jejunum as well as the stomach and duodenum. There was decreased motility of the entire bowel, so that at the end of six hours very little barium had reached the cecum. No definite organic lesion could be demonstrated.

Weight was maintained at 80 to 86 pounds until eight weeks before this admission, when the patient had a one-week episode of severe watery diarrhea with increased nausea and vomiting. The patient was admitted to another hospital, where she received three blood transfusions and the diarrhea subsided. Following this she remained so weak as to be completely bedridden, and she began to complain of numbness and tingling in the extremities and occasional cramping pain in the calves. Her weight on admission to the hospital was 70 pounds.

Physical examination was unchanged except for increased cachexia and a decline in blood pressure to 100 systolic, 58 diastolic.

The urine contained a trace of albumin and a few white cells per high-power field in the sediment. Examination of the blood disclosed a hemoglobin of 16.3 gm., a red-cell count of 5,470,000 and a white-cell count of 10,000, with a normal differential. The hematocrit was 48 per cent and the eosinophil count 75 per cu. mm. The total protein was 5.0 gm. with an albumin-globulin ratio of 1.8, the nonprotein nitrogen 17 mg., the calcium 8.0 mg., the phosphorus 2.4 mg. and the alkaline phosphatase 2.6 units per 100 cc.; the chloride concentration was 86 milliequiv., the sodium 136.1 milliequiv., the potassium 2.2 milliequiv. and the carbon dioxide 36.3 milliequiv. per liter, with a blood pH of 7.42. The blood contained 90 units of vitamin A and 50 units per 100 cc. of carotene. A glucose-tolerance test showed a fasting blood sugar of 81 mg. per 100 cc., rising to a maximum of 176 mg. per 100 cc. one hour after glucose and remaining at 157 mg. per 100 cc. two hours after sugar. The cephalin flocculation test was negative at twenty-four hours, + at forty-eight hours; the prothrombin time was 17 seconds (normal, 18 seconds). The stool contained a normal proportion of neutral fat, but soaps and other fat combinations were increased. Several stools obtained shortly after admission were guaiac positive, as were several specimens of vomitus. Stools throughout the latter part of the hospital stay were guaiac negative. An electrocardiogram revealed low voltages throughout and T-wave changes consistent with pericarditis, myxedema or diffuse coronary disease. The tracing was not characteristic of hypokalemia. X-ray films of the chest and barium-enema examination showed no new findings. A gastrointestinal series demonstrated no evidence of esophageal ulceration. The upper small bowel was dilated and sluggish, so that no barium entered the cecum twelve hours after ingestion and barium remained in the stomach twenty-four hours after the test (Fig. 2).

FIGURE 2. *Dilated Duodenum and Upper Small Bowel.*

Following admission the patient continued to vomit nearly everything taken by mouth. She

was maintained on intravenous therapy for the first two months of the hospital stay at a fairly constant weight of 70 to 75 pounds, by which time no patent superficial veins remained. It was therefore decided to perform an exploratory laparotomy and double-feeding jejunostomy. The stomach, duodenum and jejunum were dilated but not distended at operation, tapering down to apparently normal bowel in midjejunum (Fig. 3). No point of mechanical obstruction of any part of the bowel was found. The celiac ganglion was injected with 55 cc. of a 1 per cent solution of procaine. Biopsies of the jejunum were reported as slight focal degeneration and fibrosis of the circular muscle layer.

FIGURE 3. *Barium Filling Lower Small Bowel, Demonstrating Normal Caliber.*

Postoperatively the patient was maintained on high-protein, high-calorie jejunostomy feedings with Navitol and ascorbic acid added. Vomiting continued and was especially severe whenever attempts to clamp off the jejunostomy tube were made. In the seventh hospital month the patient was started on a course of testosterone, 25 mg. per day. After one month of this therapy her weight reached 79 pounds, but there was no other objective or subjective improvement. A gastrointestinal series in the eighth hospital month showed a 10-cm. smooth area of stricture in the terminal esophagus ending in a small hiatus hernia. The esophagus and stomach emptied readily to demonstrate hugely dilated second and third portions of the duodenum. After the preliminary fluoroscopy the patient vomited virtually all the gastric contents, but the barium remaining in the duodenum did not progress beyond the proximal jejunum at the end of six hours. At the end of twenty-four hours the bulk of the barium was still in the proximal jejunum.

Throughout much of the course the patient was extremely depressed, with ideas of suicide and occasional paranoid delusions concerning "electrical treatments" she believed she was receiving. In the ninth hospital month the patient was discharged to another hospital so that she might be closer to her family. Over the next nine weeks she pursued a gradual downhill course, dying quietly with no apparent acute episode six years after the onset of the first symptoms.

DIFFERENTIAL DIAGNOSIS

DR. WALTER BAUER*: May I see the x-ray films, Dr. Eyler?

DR. WILLIAM R. EYLER: The chest film shows a rather emphysematous chest, a small heart and a lack of soft tissue.

DR. BAUER: Nothing to suggest pulmonary fibrosis?

DR. EYLER: I do not see increase in linear densities other than what one would expect with this amount of emphysema. We know that we do not always recognize fibrosis. The films from the last upper-gastrointestinal series, in which the barium was followed through the small bowel and finally into the colon, show a residual change in the esophagus with narrowing of its distal end just above the hiatus hernia. An earlier examination showed ulceration in the distal esophagus just above the hiatus hernia (Fig. 1). There is atony at the stomach, dilatation of the duodenal loop and dilatation of the proximal portion of the small bowel (Fig. 2). We were never able to demonstrate any definite point of obstruction in spite of repeated fluoroscopic examinations. We have demonstrated that the distal ileum is not dilated (Fig. 3). This film shows small bowel of more nearly normal caliber. We found nothing diagnostic in the colon.

DR. BAUER: No dilation of the colon comparable to that found in the upper gastrointestinal tract?

DR. EYLER: No.

DR. BAUER: Do you think the changes in the esophagus were the result of an inflammatory process?

DR. EYLER: Perhaps secondary to a hernia.

DR. BAUER: There can be no doubt that this fifty-five-year-old woman had a malfunctioning gastrointestinal tract. The history of nausea, vomiting and severe diarrhea on at least one occasion for approximately six years and the reported gastrointestinal x-ray findings are in accord with this interpretation. The question is whether these changes were due to one disease or whether the patient had a chronic esophagitis and a separate disease of the duodenum and the small bowel. I prefer to interpret these findings as being due to one and the same disease process. I must say that I betook myself to the library to learn what other diseases or combinations of diseases might cause such extensive gastrointestinal involvement. The only disease I can think of that would explain all the findings in this case is scleroderma involving the esophagus as well as the upper gastrointestinal tract.

*Physician, Massachusetts General Hospital.

In this instance, because of the absence of cutaneous involvement, there was little to suggest the presence of scleroderma except the Raynaud's disease and the extensive changes in the esophagus and gastrointestinal tract. One notes that the symptoms of Raynaud's disease antedated those referable to the gastrointestinal tract by at least one year. This same paucity of cutaneous findings has been true of other cases of scleroderma with marked visceral manifestations. In the case under discussion there is little to suggest involvement of other systems. True, the recorded electrocardiographic changes could be due to scleroderma, as it is known that pericarditis, myocardial fibrosis and widespread lesions of medium-sized and small arteries of the myocardium are manifestations of scleroderma. Pulmonary fibrosis is another systemic manifestation of scleroderma that should always be looked for. In this case, the film of the chest does show emphysema. However, the lung markings are not sufficiently increased to permit making a diagnosis of pulmonary fibrosis.

That the visceral findings of scleroderma may appear before there are any demonstrable cutaneous changes has been reported.[1] In most of the reported cases Raynaud's disease was the first manifestation of scleroderma. Bevans[2] reported two cases that were very similar to the case under discussion except that both patients showed typical sclerodermal changes of the skin and subcutaneous tissues. In one of these cases the mucosa of the esophagus was completely replaced by fibrillar material, the submucosa was sclerotic and the muscle layers were atrophic and extremely fibrosed. Similar changes were observed in the small bowel in both cases and in the colon in one. The latter lesions were patchy in character. The other changes noted were endocardial and myocardial fibrosis, widespread vascular alterations, pulmonary fibrosis, atrophy of the thyroid and severe renal lesions. The latter were not unlike those described by Klemperer, Pollack and Baehr.[3] Bevans called attention to the fact that these cases were more severe than the clinical course and the laboratory data indicated.

In the case under discussion gastrointestinal symptoms had been present for six years, yet there was no cutaneous evidence of scleroderma other than Raynaud's disease. Similar cases have been reported by Hale and Schatzki[4] and others.[1] It should be emphasized that in the majority of these cases the Raynaud's disease antedated the gastrointestinal symptoms.

As I said previously, I know of no disease other than scleroderma that can cause such extensive involvement of the esophagus and the gastrointestinal tract as was observed in this case. I entertained the possibility of a chronic esophagitis and associated regional ileitis. However, the x-ray findings are not compatible with the latter diagnosis. Marked disturbance in the pattern of the small intestinal tract may be seen in Whipple's disease (lipophagic intestinal granulomatosis, intestinal lipodystrophy).[5, 6] This disease syndrome, characterized by sprue-like manifestations, usually accompanied by arthritis, hypotension and a secondary anemia, does not involve the esophagus. I am sure that others may suggest the possibility of chronic esophagitis with associated deficiency disease affecting the small intestine. Although I am fully aware of these and other diagnostic possibilities, I prefer to stick to the diagnosis of scleroderma involving primarily the viscera — at least the gastrointestinal tract and the heart.

Because scleroderma is a systemic disease and because the first manifestations of the disease may be due to visceral involvement, various workers have suggested terms that would indicate more appropriately the true nature of the disease. Becker,[7] in defining generalized scleroderma, specifically stated that it "is not strictly a dermatosis, but rather a disease of the connective tissue of various organs and systems, the skin, subcutaneous tissues, the muscles, bones and joints, tendons and fascias, the serous surfaces, internal organs, endocrine glands and nervous system. The patient first notices the surface alterations, consequently the dermatologist is usually first consulted."

Goetz,[8, 9] in summarizing his experience with scleroderma, wrote the following: "Obviously the term scleroderma should be abandoned. It is quite evident today that we are dealing with a systemic disease neither solely nor primarily involving the skin. Scleroderma is only the obvious and striking symptom of a generalized disease and the most serious symptoms actually arise in the viscera. Now that the visceral changes are being more widely recognized as an integral part of the disease, the systemic implications will receive much more consideration than the dermatological aspects. Physicians will be more on the look-out for these changes and undoubtedly more reports will appear in the literature. It appears therefore to the writer that now is not an inopportune time to abandon the term scleroderma which for so long has obstructed investigation into the cause of that disease and to replace it by one more descriptive of the true state of affairs. The term sclerosis already being in use, it appears that *progressive systemic sclerosis* would describe the condition adequately until such time as the etiology has been established. Scleroderma is then only one of the symptoms or signs of progressive systemic sclerosis."

DR. EDWARD B. BENEDICT: I entertained a diagnosis of scleroderma at the time of esophagoscopy, but the esophagus actually looked just like all the other cases of acute esophagitis with erosion and stricture formation such as I have seen associated with hiatus hernia, esophageal ulcer and duodenal ulcer. Dr. Sweet and I[10] reported about 60 similar cases in which esophageal biopsy showed only acute

and chronic inflammation with gastric mucosa. The pathologist did not say anything about scleroderma. I did not think we had ruled out scleroderma in this case.

DR. RICHARD SCHATZKI: How many cases of esophagitis have you seen with absence of hydrochloric acid in the stomach?

DR. BENEDICT: Very few. I had no reason to think the patient had no acid. I think the Levine tube stopped at the stricture and the esophagus was aspirated, rather than the stomach.

DR. MYLES BAKER: This patient was followed with much interest by Dr. Chester Jones after she was transferred to the medical wards about a year ago, when it became obvious that she would need long treatment. Of course she presented a time-consuming therapeutic problem to the house staff. Our reasoning followed closely that which Dr. Bauer has outlined. She was presented at the Medical Staff Rounds about a year ago and the question of scleroderma in this patient was discussed. However, we decided that we simply had to ask for surgical help since she could not survive with the available method of feeding and medication.

DR. BAUER: There are several cases reported in the literature in which an operation was performed for intestinal obstruction without the latter's being found. Bevans[2] cites one such patient with "diffuse scleroderma" who developed signs of intestinal obstruction. No point of obstruction was determined at operation, but the small intestine was diffusely dilated. Death followed in twelve hours. Permission for autopsy was not obtained.

DR. DANIEL S. ELLIS: I should like to ask Dr. Bauer how he would prove the diagnosis of scleroderma.

DR. BAUER: I do not think we can do so with absolute certainty, particularly in the absence of cutaneous changes. If the changes in the esophagus and small bowel are not sufficiently characteristic, then we cannot. My main reason for believing that this patient had scleroderma is that cases of undoubted scleroderma with extensive involvement of the gastrointestinal tract present a similar clinical picture. I think Dr. Castleman will also find fibrosis of both the myocardium and endocardium — and some degree of associated arteritis. The presence of esophageal inflammation favors the diagnosis of scleroderma. If someone asked: "Can you rule out dermatomyositis?" I would have to say "No," but would hastily add that if this was dermatomyositis it simulated scleroderma.

DR. BENJAMIN CASTLEMAN: In the cases that you looked up, Dr. Bauer, were there any without involvement of the skin?

DR. BAUER: Yes.* In Soma Weiss's study of sclerodermal heart disease the appearance of cardiac symptoms preceded the cutaneous changes by as much as two years. There is also on record one case in which the gastrointestinal involvement was present five or six years before the typical cutaneous lesions of scleroderma became evident.

*See References 1, 4, 8 and 11.

CLINICAL DIAGNOSIS

?Scleroderma.

DR. BAUER'S DIAGNOSIS

Scleroderma.

ANATOMICAL DIAGNOSIS

?Scleroderma of esophagus and small intestine.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The most interesting specimen in this case was the biopsy specimen of jejunum removed by Dr. Arthur W. Allen. The jejunum showed a great deal of degeneration of the circular layer of muscle fibers. In looking it over again this morning I noted that the ganglion cells of the nerves had degenerated to a great extent, a finding that has been reported in a number of cases of scleroderma of the small bowel as well as of the esophagus. There is no doubt of actual disease in the wall of the jejunum, but the question is whether it could possibly have been a secondary manifestation, and that I am unable to answer.

The autopsy showed one of the most severely cachectic persons that we have ever examined — she weighed less than fifty pounds. Every organ in the body was very small. The skin was markedly atrophic but did not have the thickened appearance that we see in scleroderma. Although the microscopical sections of the skin showed very severe atrophy of fat so that the fibrous connective tissue between the fat lobules appeared quite prominent, I am not at all sure that there was any increase in fibrosis — certainly not of the corium or the subcutaneous tissue. A mucoid degeneration of the fat tissue that is quite often seen in so-called group diseases was found, but I am not sure we cannot see it only in atrophy of fat. There was also a slight cellular infiltration in an occasional section of the skin, but looking at that slide alone one certainly would not want to say it was scleroderma. The upper two thirds of the esophagus was normal; the lower third showed a very severe esophagitis, which I believe is nonpathognomonic. I do not believe I can say it was or was not scleroderma. The entire mucosa was gone and the wall was thickened. There was no actual degeneration of the muscular layers of the esophagus. The small bowel was paper-thin; if one handled it too roughly I am sure one would tear it. Microscopically in the small bowel one could see a very thin layer of muscle and mucosa. That is all there was. Everything was so atrophied

that I do not see how anybody can say what the lesion was. Unfortunately the other organs of the body did not show anything that would make one think of scleroderma. The heart was small, weighing only 100 gm., and showed no areas of fibrosis. The lungs were emphysematous, with some fibrosis. This may be a clue to the diagnosis of scleroderma, but the fibrosis was minimal. The kidneys did not show anything of note.

A few vessels, throughout the body were slightly thickened; in one or two vessels when we looked very hard, we thought we saw some mucoid degeneration, but we were hard put to it to make a diagnosis of scleroderma. We thought it could well be scleroderma; but on the other hand it is possible that this started out as an ulcer of the esophagus, with the hiatus hernia, which would go together. We did not find a duodenal ulcer. If we had found one we could perhaps have built up the whole syndrome. We know that this patient had had some psychic trauma; could anorexia nervosa in combination with not eating have led to this severe cachexia — and explain the changes in the small bowel?

DR. BAUER: On the basis of deficiency disease?

DR. CASTLEMAN: Yes. Dr. Schatzki, will you tell us if you have ever seen changes like these in the small bowel resulting from a deficiency condition alone? Could you explain it in any way without bringing in scleroderma?

DR. RICHARD SCHATZKI: When Dr. Castleman talked to me on the telephone about this case, he was somewhat doubtful about a diagnosis of scleroderma. There were a few findings that were a little unusual for scleroderma. Of course one hesitates to make such a diagnosis without involvement of the skin. On the other hand, as Dr. Bauer said, scleroderma has been proved to be not only a disease of the skin but also a disease of most of the tissues of the body; therefore it is not unreasonable to assume that occasionally the skin would be spared. Raynaud-like changes in the skin often take the place of actual sclerodermal changes. In other words, the frequency of Raynaud's disease in scleroderma is so common that one is forced to assume that they are probably the same disease or at least have something to do with each other. The other finding that is a little unusual in this case is the extent of the lesions in the esophagus. Most of our cases of scleroderma have shown not so much esophagitis with stricture but merely atony with absence of peristalsis. Some cases have shown areas of esophagitis with stricture but usually only very small areas were involved. Some of the cases in the literature were more extensive, but I do not know of any case with as long a stricture as this patient had. That may be only a matter of degree; judging from the rest of the findings, I think it was the most extensive case of esophagitis in scleroderma that I know of.

In favor of scleroderma are the changes in the small bowel. I have seen marked distention of the duodenum in many diseases. Marked distention of the duodenum is not a pathognomonic sign of scleroderma, as it may occur in any debilitated patient. Patients with tuberculosis show it. In a series of patients with pulmonary tuberculosis that I reviewed, many showed some atony, but I have never seen the atony extend so far down into the small bowel in such cases. A simple deficiency pattern can produce all kinds of small-bowel changes, as you know. However, I doubt that it would produce such atony without any true mucosal changes. Usually there is some constriction with the atony. The description of the operation sounds almost identical with one Dr. Sweet performed seven years ago on a patient who seemed clinically to have a mechanical obstruction in the jejunum. At operation the jejunum was markedly dilated, and it tapered off gradually into normal bowel. A piece of small bowel that was resected showed nothing characteristic histologically. That patient had scleroderma of both hands. Although some of the findings in the case under discussion are new to me, I shall vote in favor of scleroderma.

Did this patient show any perivascular infiltration?

DR. CASTLEMAN: Not much.

DR. BAUER: Was arteritis seen in the biopsy specimen?

DR. CASTLEMAN: No; only a focal degeneration of the muscle. I do not know that we can solve this problem entirely, but the more I studied the slides this morning, the more I tended toward scleroderma.

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CASE 37152

Presentation of Case

First admission. A forty-four-year-old woman was admitted to the hospital because of moderately severe right-upper-quadrant pain.

One year before entry the patient began to have attacks of right-upper-quadrant pain lasting two or three days. The pain was "squeezing" in character, did not radiate and was not related to any special food or time of day but was generally worse during the night. There was no associated jaundice. Bicarbonate of soda relieved the pain within a few minutes. There was no nausea, vomiting nor change in the color or character of the stools. These episodes recurred at intervals of two to three months. Between attacks she considered herself to be in good health. However, she had noticed that she had felt increasingly tired in the few weeks prior to admission, but she attributed this to an increase in her work. One week prior to admission she developed a progressively severe headache, accompanied by dizziness, which forced her to go to bed. Three days before entry the headache seemed much less severe, but she noted moderately severe right-upper-quadrant pain similar to that noted in previous attacks that persisted without appreciable change until the time of admission. She noted no jaundice nor changes in her stools. She had lost 13 pounds while on a diet six to eight months prior to admission. However, she had discontinued the diet after two or three months and had regained several pounds.

There was no history of previous serious illnesses.

Physical examination showed a well nourished woman lying quietly in bed, in no apparent distress. The heart and lungs were negative. The abdomen was soft and nontender and there were no palpable masses.

The temperature was 99°F., the pulse 100 and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

A urine examination showed a ++ test for albumin and no sugar. Examination of the blood disclosed a hemoglobin of 5.6 gm., a red-cell count of 2,930,000 and a white-cell count of 5500, with 77 per cent neutrophils. The nonprotein nitrogen was 27 mg., the total protein 5.8 gm. and the amylase 32 units per 100 cc. The prothrombin time was 19 seconds (normal, 17 seconds). A stool guaiac test was negative. A gastrointestinal barium series showed only prominent gastric rugae. A barium-enema examination was negative. Several films showed regions of calcification in the right upper quadrant.

While the diagnostic procedures were being carried out she was given several transfusions and showed marked improvement in strength and color. The hemoglobin on the fifth hospital day was 12.2 gm. The pain gradually decreased. The aspirated contents of the stomach gave a negative guaiac test and contained 11 units of free hydrochloric acid.

On the sixth hospital day a laparotomy was performed. The gall bladder was found to contain two large calculi and was removed. The common duct was explored and appeared negative. The entire gastrointestinal tract was explored and no abnormalities were demonstrated except questionable thickening of the stomach wall.

The postoperative course was uneventful except for a rise in temperature on the first postoperative day to 102°F. However, this rapidly subsided and she was discharged on the seventeenth hospital day.

Final admission (one month later). The patient was readmitted because of jaundice of two days' duration.

She had felt well for two weeks after discharge and had regained strength. However, at the end of the two weeks she again began to feel weak. She was given liver injections by her doctor, with little improvement. She had no pain but did have slight epigastric distress after evening meals. Four days prior to admission she noted that the urine was dark and that the stools were lighter than usual. On the day prior to admission she noted that she was jaundiced. She had no acute abdominal pain and no chills or fever.

Physical examination showed a moderately jaundiced woman in no acute distress. The heart and lungs were negative. The liver was palpable 4 cm. below the costal margin on deep inspiration and was not tender. The margin was sharp. The spleen was not palpable. A pelvic examination showed the uterus to be slightly enlarged and firm.

The temperature was 98.6°F., the pulse 90 and the respirations 20. The blood pressure was 140 systolic, 80 diastolic.

The urine had a specific gravity of 1.010 and gave a + test for albumin. Examination of the blood showed a hemoglobin of 13.6 gm. and a leukocyte count of 5100, with 69 per cent neutrophils. The prothrombin time was 21 seconds (normal, 17 seconds). The serum albumin was 4.94 gm., the globulin 2.77 gm. and the alkaline phosphatase 3.5 units per 100 cc. The cephalin flocculation was ++ in forty-eight hours. The urine urobilinogen was 4.35 Ehrlich units.

The jaundice deepened after admission. She complained of being awakened by pruritus on the third hospital day. On the fourth hospital day she passed a brown stool. It was noted that the respirations were marked by deep sighing, but otherwise her condition remained unchanged. By the sixth hospital day the jaundice had deepened further, and she complained of weakness and nausea. The urine urobilinogen at this time was 0.98 Ehrlich units. The hemoglobin was 11.8 gm. and the leukocyte count 6000. The sedimentation rate was 23 mm. in sixty minutes. The serum bilirubin was 18.0

mg. direct and 24.4 mg. per 100 cc. indirect. The cephalin flocculation was +++ in forty-eight hours.

On the seventh hospital day she passed a stool that was somewhat lighter than the one passed on the fourth hospital day, which still had some color. Her general condition showed little change. On the tenth hospital day an operation was performed.

Differential Diagnosis

Dr. Richard Warren*: I wonder if we might look at the x-ray films at this time, Dr. Hanelin?

Dr. Joseph Hanelin: All the x-ray films that we have were made at the time of the first admission.

The barium-enema examination was entirely normal. We made two examinations of the upper gastrointestinal tract, two days apart. The esophagus appears normal. The stomach shows prominent folds, and there is some suggestion in the first examination that there is an ulcer along the lesser curvature of the stomach near the fundus, but this is disproved by the examination made two days afterward. The stomach is rather peculiarly placed, being sharply folded upon itself at the angle so that the pylorus lies only slightly below the level of the fundus. This may be an anatomical variant and is not necessarily important. The duodenal loop is somewhat wide, but this can be explained by the peculiar position of the stomach. There is no evidence of a duodenal ulcer. Two gallstones are visible in the right upper quadrant.

Dr. Warren: Was there a hiatus hernia?

Dr. Hanelin: No.

Dr. Warren: Can you enlarge on the finding of the prominent gastric rugae?

Dr. Hanelin: The prominent rugal folds suggest the presence of gastritis.

Dr. Warren: Was a cholangiogram done after the first operation?

Dr. Hanelin: No — and no films were taken during the second admission.

Dr. Warren: One diagnosis is obviously easy to make: namely, gallstones. Whether there are one or two additional diagnoses is the big question to decide. The two things besides the gallstones that draw my attention in this history are the anemia the patient had when she first came in and the jaundice that occurred about six weeks after cholecystectomy.

*Assistant surgeon, Massachusetts General Hospital.

I shall discuss the anemia first. There was very little in the record to help me to decide the type of this anemia. In any patient with gallstones and anemia, I should like to have a fragility test, perhaps a reticulocyte count and a few more hematologic studies of that type. There was no jaundice, however, prior to operation, and the character of the postoperative jaundice was such that I do not need to consider hemolytic anemia. Primary anemia is excluded by the presence of acid in the stomach.

Obviously the clinicians were worried about the gastrointestinal tract as a source of hemorrhage to explain the anemia. There was no history of tarry stools or gastrointestinal bleeding. There was no positive test for occult blood in the stools on one examination in the hospital. However, when the surgeons examined the gastrointestinal tract from top to bottom at operation they obviously were looking for some local lesion. The information I have been given about the operation also leaves something to be desired. I wonder if it is fair to ask about the condition of such organs as the spleen, liver and pancreas at the time of operation? I should also like to know if anything abnormal was found when the common bile duct was explored.

Dr. Daniel S. Ellis: The surgeon who operated on this patient is not present. I did not see the patient until the second admission. I was told there were no abnormalities, other than those in the gall bladder.

Dr. Warren: Thank you very much.

It is often difficult to be sure about the presence of a duodenal or gastric ulcer by examining the outside of the stomach at operation; that is why, when a patient is operated on for bleeding and the external appearance of the gastroduodenal segment is negative, surgeons look inside to be sure there is no bleeding point. The same may be true of a lesion of the ampulla of Vater — and a small lesion there is often very difficult to feel. I am skirmishing around in order to try to tie up the cause of the bleeding with that of the jaundice. Among such causes of gastrointestinal hemorrhage are duodenal ulcer encroaching on the biliary passages and carcinoma of the ampulla of Vater. Either lesion may have been missed at operation. I think both are unlikely here, but I must mention them.

One of the interesting points is that the anemia did not recur after the cholecystectomy. The anemia was relieved by transfusions and apparently

cured by cholecystectomy, at least for a period of six weeks. I do not know what that means. Bleeding from gallstones does occur. I have seen a patient who had anemia and whose gall bladder and biliary tree were full of blood at operation. There was no anatomic explanation for it. Most bleeding from the biliary tree comes from intrahepatic bleeding or bleeding from an aneurysm of the hepatic artery, but bleeding from gallstones is so rare that it is almost impossible to make the diagnosis clinically. I shall vote against that cause of bleeding here. Something slightly abnormal was reported in the stomach. I shall have to grasp this thin reed, and shall classify the cause of the bleeding, if it occurred at all in this case, either in the group of gastritis or, possibly, in the group in which the source is never found. In gastrointestinal clinics, in about 10 or 15 per cent of patients who bleed from the upper gastrointestinal tract the source of the bleeding is never found. Remember, I am assuming the anemia is due to hemorrhage, although I have no evidence for that.

Now to consider the cause of the jaundice. This jaundice was painless; it came on after a prodromal period of two weeks of upper-gastrointestinal symptoms that may or may not have been related to the gall-bladder operation; it was not accompanied by fever. It was first accompanied by stools containing bile — even in the last stool, although it was clay colored, some bile seemed still to be present. The urobilinogen determinations showed that the bile was getting into the gastrointestinal tract at the beginning of the course but that it later became diminished. The question arises whether this was obstructive jaundice in which the bile was getting into the intestinal tract intermittently, as occasionally occurs because of a ball-valve stone in the common duct or a tumor near the ampulla of Vater, or whether this was an intrahepatic type of jaundice in which the hepatic disease was progressive and the excretion of bile less and less. I do not have much evidence one way or the other from the laboratory point of view. The cephalin-flocculation tests were not strongly in favor of intrahepatic disease and the alkaline phosphatase was not strongly in favor of obstructive jaundice. I think, on the law of averages — and in these conferences one has to play the percentages — that the chances of this having been extrahepatic biliary obstruction are poor. It is true that some cases of extrahepatic obstruction come on gradually like this, with progressively less bile going into the intestinal tract — but it is unusual, and I should vote in favor of intrahepatic disease.

The operation that was performed on the tenth hospital day bothers me somewhat. I would have thought, on the evidence presented here — if this was truly an operation and not a liver biopsy — that the operation might have been postponed somewhat longer. However, I am supposed to use not that type of reasoning but merely the evidence I have been given. I guess that the patient had homologous serum jaundice induced by the transfusion and not any so-called surgical type of jaundice. I guess she had, as the cause of the anemia (and that is much more of a guess to my mind than the diagnosis of homologous serum jaundice), perhaps a gastric ulcer or chronic gastritis. It may also be that the cause of the anemia at this stage of the clinical course was not discovered.

Dr. Jacob Lerman: Why the drop in urobilinogen? Can you explain that?

Dr. Warren: When patients with severe liver damage completely shut down and bile stops getting into the gastrointestinal tract, there is a diminution in the urobilinogen in the urine.

Clinical Diagnosis

Serum hepatitis.

Dr. Warren's Diagnoses

Homologous serum jaundice.
?Gastric ulcer or chronic gastritis.

Anatomical Diagnosis

Viral hepatitis, severe (homologous serum).

Pathological Discussion

Dr. Tracy B. Mallory: The second operation, which was in prospect at the point where the protocol ends, was a needle biopsy of the liver and was performed by Dr. Ellis. This showed evidence of very severe liver disease, with rather more liver-cell necrosis than the average case of hepatitis shows but not more than is consistent with that diagnosis, so that it was reported as severe viral hepatitis. There is no histologic distinction between the so-called epidemic type of hepatitis and that of homologous serum jaundice. The histologic picture is identical in both conditions. Moreover, until we have an

experimental animal to which the disease can be transmitted, with protection tests being made, it will be impossible, except on epidemiologic grounds, to distinguish between these two very similar diseases, if they are two diseases.

A few years ago, in Scandinavia, reports began to appear of an unusual number of cases of hepatitis in women at or beyond the menopause, with a very high case-fatality rate.* Whether this was due to an unusual strain of the virus or whether the sex and age were responsible for the exceptional severity of the disease was never clearly settled. Because of those case reports considerable concern was felt about this patient. It was believed that she might run a very severe clinical course and that there was actually some danger of a fatal outcome. However, she made a very satisfactory recovery. I shall ask Dr. Ellis to tell you about that. Another liver biopsy done three months later showed complete restitution to normal of the liver tissue.

DR. ELLIS: I should like to congratulate Dr. Warren on being 100 per cent correct in his diagnoses — including the last one he made, that the source of the anemia would not be determined. At the present time (nine months later) the patient has been in the hospital again for ten days with exactly the same history that brought her here on the first admission. Down to every detail the first paragraph of the protocol can be repeated. She did recover from the hepatitis after three months in the hospital and two months at home, during which time she maintained a hemoglobin between 12.5 and 13.5 gm. without any difficulty. She gained 25 pounds and began to be up and around and has had follow-up study in the office. In the past four weeks, however, she began to have gastrointestinal symptoms — epigastric distress and pain at night, relieved by soda. Four weeks ago she had a hemoglobin of 11.5 gm., yet three weeks ago she was admitted to the hospital with a hemoglobin of 5.5 gm.

You wanted to know about certain other tests. The bone-marrow biopsy showed some hyperplasia of red-cell elements, the fragility test was normal and the reticulocyte count was 5 per cent. At the present time she has some free acid in the gastric secretions. She is not jaundiced, the liver-function tests are normal, the liver is two fingerbreadths below the costal margin and the spleen in not palpable.

Now that you have all the information, perhaps you will tell me why she has anemia and why she has the gastrointestinal symptoms?

DR. WARREN: Did you say she had no history of gastrointestinal bleeding?

DR. ELLIS: None whatever. We have another gastrointestinal series that is normal.

DR. HANELIN: It is identical with the first set. Dr. Ellis, was any explanation of the position of the stomach discovered at the time of the laparotomy?

DR. ELLIS: Not to my knowledge. I was not present at the operation.

DR. ALLEN G. BRAILEY: Would you assume that she is bleeding from somewhere?

DR. ELLIS: No.

DR. BRAILEY: Then she has not been forming blood!

DR. ELLIS: We have no evidence that she could not form blood. We assume that she is hemolyzing it somewhere.

DR. MARIAN ROPES: Did you have a van den Bergh test made at the time the urobilinogen dropped?

DR. ELLIS: No.

DR. WARREN: Was a Coombs test done?

DR. ELLIS: A Coombs test was negative.

*Jersild, M. Infectious hepatitis with subacute atrophy of liver. *New Eng. J. Med.* 237:8-11, 1947.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society
Owned by the Massachusetts Medical Society and Published Weekly under the Jurisdiction of the Committee on Publications

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Subscription Terms: $8.00 per year in advance, postage paid, for the United States (medical students, $4.00 per year); Canada, $9.00 per year (Boston funds); foreign, $10.50 per year.

Microfilm volumes available to regular subscribers through University Microfilms, 313 N. First Street, Ann Arbor, Michigan.

Material, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

"GIVE TO CONQUER CANCER"

The analysis by Clarence L. Scamman, medical director of the American Cancer Society, Massachusetts Division, of suspected cases of cancer of the lung, published elsewhere in this issue of the *Journal*, is another reminder of the significance of April in America's calendar of charitable undertakings.

Following closely on the heels of the Red Cross campaign in March, the Easter-seal sale of the Bay State Society for the Crippled and Handicapped, the appeal of the American Heart Association in February and the March of Dimes in the same month, April is devoted to the very real needs and problems of the American Cancer Society.

The growing importance of cancer among the diseases of mankind justifies the belief of those in charge of the policies of the Society that there is a different — a particularly dramatic — urgency to their appeal that distinguishes it from all others. One factor in this distinction, which applied also to the campaign of the American Heart Association, is that a major part of the funds obtained is used for research and a program of education in the control of the disease.

The share of the Massachusetts Division of the American Cancer Society in the raising of funds this year is $530,166.

The objectives of the American Cancer Society are approved, and their full support is urged on the public — even though one wishes that all these special campaigns that importune the public with such insistence might be better co-ordinated one with the other.

One suspects that all might better serve their basically unselfish purposes if they could plan their money-raising activities with the purposes of each other and United Community Services more clearly in mind.

It is more than a matter of generosity; it is a matter of common sense that the American Cancer Society should receive the full support of the people of this country, but it is also, in the long run, a matter of ordinary intelligence that agencies devoted to the public welfare should plan their activities in a spirit of mutual efficiency.

THE BAY STATE MEDICAL REHABILITATION CLINIC, INCORPORATED

The announcement of the establishment of the Bay State Medical Rehabilitation Clinic, Incorporated, at the Massachusetts General Hospital should be welcome news to the physicians, surgeons and hospitals of the community, as well as to various social agencies concerned with the care of injured, diseased or physically handicapped persons. The need for such a service has been quite apparent for several years, particularly in view of the growing realization that the physician's responsibility does not end with definitive medical or surgical care but extends into the third phase of medicine, which ceases only with the returning of the patient to

that place in the community in which he can live most fully and usefully.

The majority of physicians and surgeons are probably not familiar with this sphere of practice, as undergraduate medical education has been lacking in this aspect of treatment. Only recently, through organized postgraduate training, a medical specialty has developed that is known as physical medicine and rehabilitation. Specialists in this field, known as physiatrists, concentrate on this portion of medical practice and prescribe specific therapy at the hands of physical and occupational therapists and other ancillary medical technicians. The Bay State Medical Rehabilitation Clinic is primarily dedicated to providing proper continuity of medical care through this "third phase." The service is in reality physical medicine in its fullest sense, which includes medical rehabilitation. The center will not duplicate facilities already available to the community but aims to provide a new type of service — *medical rehabilitation.* This is not to be confused with vocational rehabilitation, which does not require the same intimate daily medical direction. Several other local agencies have facilities for vocational guidance and training, and they will be called on by the center as indicated.

To provide this medical rehabilitation service, the professional staff will include a director who is a specialist in physical medicine and rehabilitation, physical and occupational therapists experienced in the technics of physical restoration and analysis and development of occupational skills, and a medical social worker trained in counseling and co-ordination of rehabilitation activities. Space is available for an occupational-therapy shop, with facilities for testing skills, and a gymnasium for physical therapy. Special diagnostic examinations will be readily available at the Massachusetts General Hospital when needed, without duplication of expensive equipment. Specialized types of treatment, including speech therapy, hydrotherapy and electrotherapy, may also be obtained. A large board of consultants from the many teaching hospitals of the city will provide expert opinions in all the special medical fields.

Another important function of the center will be education, particularly in the ancillary medical services such as physical and occupational therapy, medical social service, orthopedic nursing and training of residents in physical medicine and rehabilitation. It is hoped also that a certain amount of clinical research in this new specialty will be developed.

It is anticipated that the majority of patients who will receive benefit at the center will be those who have had industrial accidents, amputations and fractures and sufferers from arthritis and neuromuscular disabilities.

Although located in a building on the grounds of the Massachusetts General Hospital and thus benefiting by the close proximity to the facilities of this outstanding hospital and teaching and research center, the Bay State Medical Rehabilitation Clinic is a completely independent nonprofit corporation, aided by anonymous gifts and backed by the Bay State Society for the Crippled and Handicapped. It hopes to provide a new and important community medical service deserving the co-operation and approbation of the medical profession.

"— OUR FEVERISH WAYS — "

THE inhibitory effect of heat on the animal economy was suggested not long ago by Mills,[1] who presented several reasonable arguments in favor of the theory. Professor Mills' contention that whether the subjects are college students or beef cattle heat slows them up, was not refuted; his observations were mentioned in these columns[2] and the matter was considered closed.

New light has been shed on the subject, however, by A. E. Hotchner,[3] viewing it from the angle of the internal environment. This author, writing in no less authoritative a medium of publicity than *This Week Magazine*, indicates that the productive capacity of the individual, his verve, his lightheartedness and his general social acceptability vary directly with his body temperature.

Human beings, moreover, according to Dr. Nathaniel Kleitman of the University of Chicago, who made the observations, are divided into three groups: Group A, consisting of those whose temperature is highest and whose productivity is greatest in the forenoon; Group B, those persons whose temperature reaches its peak in the afternoon; and Group C, composed of those who have a morning and an evening rise. They might be appropriately classified as the larks, the owls and the bactrians, identified by their two humps.

This recognition of man's febrile periodicity gives him an opportunity to plan his work so that his really exacting tasks can be performed when his internal flame is at its most incandescent point. In this way, also, he can avoid consuming his candle too quickly by burning it at both ends.

Man is not entirely a victim of his febrile fate, however, for his temperature can be trained to suit its host, first by gentle firmness in respect to the matter of bedtime, and secondly by elevating it at the right time through judicious exercise or the less strenuous means of hot showers and heating pads.

The factor of the external environment thus comes into play, indicating a possible inconsistency between the two theories.

References

1. Mills, C. A. Temperature dominance over human life. *Science* **110**: 267-271, 1949.
2. Editorial. Heat versus vigor. *New Eng. J. Med.* **241**:884, 1949.
3. Hotchner, A. E. When your temperature goes up. *This Week Magazine*, Dec. 17, 1950. P. 18.

GOING UP!

Fifty million Frenchmen, it has been said, can't be wrong, and the aphorism has been trimmed down to apply to a tenth of one per cent of the same number of freshmen.

On March 22 the *Journal*, by discarding only another cipher — a mere nothing, was able to apply the same standards of infallibility to nearly 20 per cent of the medical students of the nation. On that date the number of the *Journal's* undergraduate subscribers stood at exactly 5000, representing a steady increase since the academic year began — and a gain of 417 over the corresponding date of 1950.

The editors pay their respects to these loyal adherents and hope to merit their continued support.

The eighth annual report of the managers of the State Lunatic Asylum of New York has been received. We have never perused any similar report with more pleasurable satisfaction. . . . Total number (of patients) during the year, 816. — Of this number there has been discharged; — Recovered, 171; much improved, 8; improved, 49; unimproved, 108; died, 51.

Boston M. & S. J., *April 16, 1851*

NOTICES

BOSTON CHAPTER OF AMERICAN FEDERATION FOR CLINICAL RESEARCH

A meeting of the Boston Chapter of the American Federation for Clinical Research will be held in the Massachusetts Memorial Hospitals on Monday, April 16, at 8 p.m.

Program

Studies on the Relationship of Serum Cation Concentration to Electrocardiographic Abnormalities. Drs. J. P. Merrill, J. M. Weller, M. G. Criscitiello, H. D. Levine and B. Lown. Peter Bent Brigham Hospital and Harvard Medical School.

Some Endocrine Functions in Graves' Disease. Drs. Farahe Maloof and Bernard Stall, III. Massachusetts General Hospital.

The Volume and Distribution of Blood in the Leg with Special Reference to the Prophylaxis of Thromboembolism. Drs. Julius Litter and J. Edwin Wood, III. Massachusetts Memorial Hospitals.

The Turnover Rate of Human Serum Albumin as Measured by I^{131}-Tagged Albumin. Drs. Kenneth Sterling and Seymour J. Gray. Biophysical Laboratory and Department of Medicine, Harvard Medical School, and the Medical Clinic, Peter Bent Brigham Hospital.

The Nephrotic Syndrome in Children: Inferences Regarding the Renal Lesion and Mechanisms of ACTH-Induced Diuresis Based on Clearance Techniques. Drs. J. Metcoff, C. P. Rance, N. Nakasone and C. A. Janeway. Children's Hospital.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Conference Program
9–10 A.M.

Tuesday, April 17 — Advances in Ophthalmology from a General Medical Standpoint. Dr. Joseph Igersheimer.

Wednesday, April 18 — Radioactive Iodine in Thyroid Disease. Dr. Ray E. Persons, Jr.

Friday, April 20 — The Electron Microscope and Some of Its Applications to Biological and Medical Research. Dr. Harrison Latta.

Tuesday, April 24 — X-ray Conference. Dr. Alice Ettinger and Staff.

Wednesday, April 25 — Hematology Clinic. Dr. William Dameshek.

Friday, April 27 — Oral Lesions Indicative of Systemic Disease. Dr. Harold J. Jeghers.

Conferences are held in the Pratt Lecture Hall.

All exercises are open to the medical profession.

ORTHOPEDIC SEMINARS

Dr. Charles O. Bechtol, of the University of California, will present the following orthopedic seminars in the Bigelow Amphitheater, White 3A, Massachusetts General Hospital, at 5 p.m.

Tuesday, April 17 — Fundamental Studies on Locomotion.

Wednesday, April 18 — Clinical Muscle Physiology and Evaluation of Gait.

Interested physicians are cordially invited to attend.

SOUTH END MEDICAL CLUB

The annual hospital meeting of the South End Medical Club will be held at the Peter Bent Brigham Hospital, on Tuesday, April 17.

NEW ENGLAND CARDIOVASCULAR SOCIETY

The next meeting of the New England Cardiovascular Society will be presented by the staff of the Children's Medical Center at New England Mutual Hall, 225 Clarendon Street, Boston, on Monday, April 23, at 8 p.m., Dr. Benedict F. Massell presiding.

Program

A Note on the P-R Interval in Sinus Arrhythmia. Drs. Otto F. Ehrentheil, Mariano M. Alimurung and Benedict F. Massell.

Paroxysmal Tachycardia in Infants and Children: A Review of 40 Cases. Drs. Alexander S. Nadas, William C. Daeschner and Arthur Roth.

The Roentgenographic Findings in Congenital Tricuspid Atresia with Hypoplasia of the Right Ventricle. Drs. Edward B. D. Neuhauser and Martin H. Wittenborg.

Antibody Response to Non-Streptococcal Antigens as Related to Rheumatic Fever Susceptibility. Drs. Joseph M. Miller, Sidney Kibrick and Benedict F. Massell.

The Defense of Aortic Pressure Head in Congenital Heart Disease. Drs. James W. Dow and Richard Gorlin.

The Seasonal Occurrence of Patent Ductus Arteriosus. Drs. David D. Rutstein, Rita J. Nickerson and Felix P. Heald.

Present Status of Penicillin Prophylaxis of Rheumatic Fever. Drs. Benediet F. Massell and George P. Sturgis.

Interested physicians and medical students are cordially invited to attend. (*Please note place of meeting.*)

NEW ENGLAND DEACONESS HOSPITAL

The following staff meeting and clinics will be held in the Baker classroom of the New England Deaconess Hospital.

April 24. 5:00 p.m. Value of Routine Chest X-rays in Practitioner's Office, in Hospital and in Community. Dr. Joseph H. Marks.
Three chest cases illustrating surgery and pathology. Drs. C. C. Miller, R. Overholt, F. H. Lahey and William Meissner.
April 27. 8:15 a.m. Diabetic Coma. Dr. Howard F. Root.
10:30 a.m. Diabetes. Dr. Elliott P. Joslin.
Physicians are cordially invited to attend.

BOSTON CITY HOSPITAL ALUMNI ASSOCIATION

Alumni Day of the Boston City Hospital Alumni Association will be held Saturday, April 28, 1951.

Clinical Program: Medical Section

(Cheever Amphitheatre, Dowling Building. Dr. Max Ritvo presiding.)

9:15–9:45 a.m. Experiences with the Newer Anticoagulants. Dr. William C. Moloney.
9:45–10:15 a.m. Untoward Reactions from the Therapeutic Use of Morphine. Dr. Harold J. Jeghers.
10:15–10:45 a.m. The Shoulder-hand Syndrome Following Myocardial Infarction. Dr. John P. Rattigan.

Recess

11:00–11:30 a.m. Color Photography in the Field of Medical Evidence. Dr. Richard Ford.
11:30 a.m.–12:00 m. Treatment of Acquired Hemolytic Anemias. Dr. William B. Castle.
12:00 m. The General Leonard Wood Oration: The Use of Antibiotics. Dr. Chester S. Keefer.

Clinical Program: Surgical Section

(Mallory Amphitheatre. Dr. William Reid Morrison presiding.)

9:15–9:45 a.m. Pulmonary Function Studies and Surgical Problems. Dr. John W. Strieder.
9:45–10:15 a.m. Surgical Treatment of Skin Lesions, including Traumatic Contractures and Pigmented Naevi. Dr. V. H. Kazanjian.
10:15–10:45 a.m. Herniation of the Temporal Cortex through the Incisura of the Tentorium: Diagnosis and Treatment. Dr. Donald Munro.

Recess

11:00–11:30 a.m. The Action of Drugs on the Biliary Tract. Dr. John M. McGowan.
11:30 a.m.–12:00 m. Opaque Shadows Resembling Ureteral Calculi. Dr. George C. Prather.
12:00 m.–12:30 p.m. Cancer Research. Dr. C. P. Rhoads.
12:30 m.–1:00 p.m. Partial and Complete Pelvic Exenteration for Advanced Cancer: Progress Report. Dr. Alexander Brunschwig.

Clinical Program: Sixth Surgical (Orthopedic) Service

(Thorndike Amphitheatre. Dr. Russell F. Sullivan presiding.)

9:15–9:30 a.m. Introductory Remarks. Dr. Russell F. Sullivan.
9:30–9:45 a.m. Joseph H. Shortell: a biographical sketch. Dr. Otto J. Hermann.
9:45–10:00 a.m. Fatigue Fractures. Dr. Ronald W. Adams.
10:00–10:30 a.m. Slipped Capital Femoral Epiphysis: Recent Advances in Detecting Early Slipping. Dr. Robert J. Joplin.
10:30–10:50 a.m. Fractures of Anterior Lip of Os Calcis. Dr. Charles H. Bradford.

Recess

11:00–11:30 a.m. Fracture-Dislocations of the Astragalus. Dr. Paul O'Brien.
11:30 a.m.–12:00 m. Fractures of the Proximal Tibial Epiphysis. Dr. Alexander P. Aitken.
Fractures of the Distal Femoral Epiphysis. Dr. H. Kelvin Magill.
12:00 m. Dupuytren's Contracture (motion picture). Dr. J. Edward Flynn.

Afternoon Program

1:00–2:00 Luncheon for all members of the Alumni Association, House Officers' Dining Room, courtesy of the Board of Trustees, Boston City Hospital.
2:00–5:00 Visits to the operating rooms and wards. Inspection of the new Fracture Wing in the Dowling Building.

Evening Program

6:00 Annual meeting.
6:30 Cocktails.
7:00 Annual banquet.

VALLEYHEAD HOSPITAL

The annual meeting of the Valleyhead Hospital will be held at the hospital, 20 South Street, Carlisle, Massachusetts, on Tuesday, April 17, at 8 p.m. This meeting is held in connection with the third anniversary of the founding of the hospital.

Dr. Mark D. Altschule will speak on the subject "Physiological Observations in Mental Diseases." A general discussion will follow and a collation will be served.

Interested physicians are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

April 15. Council of the New England State Medical Societies. Page 535, issue of April 5.
April 16. Massachusetts Physicians Art Association. Page 536, issue of April 5.
April 16. Boston Chapter of American Federation for Clinical Research. Page 575.
April 17-27. Joseph H. Pratt Diagnostic Hospital. Page 575.
April 17. Orthopedic Seminar. Page 575.
April 17. South End Medical Club. Page 575.
April 17. Valleyhead Hospital. Notice above.
April 18. Greater Boston Medical Society. Page 535, issue of April 5.
April 18. Physical Medicine and Rehabilitation in Psychiatry. Dr. Walter E. Barton. New England Society of Physical Medicine. Hotel Kenmore. 8 p.m.
April 18. Orthopedic Seminar. Page 575.
April 20. Niles Memorial Lecture. Page 458, issue of March 22.
April 20. Boston Surgical Society. Page 494, issue of March 29.
April 20. New England Deaconess Hospital. Page 535, issue of April 5.
April 21. Massachusetts Association of Medical Technologists. Page 494, issue of March 29.
April 23. New England Cardiovascular Society. Page 575.
April 24. New England Deaconess Hospital. Notice above.
April 24. Norfolk District Medical Society. Page 629, issue of October 19.
April 25. Naval Reserve Volunteer Medical Unit No. 1-1. Page 535, issue of April 5.
April 27. New England Deaconess Hospital. Notice above.
April 28. Boston City Hospital Alumni Association. Notice above.
April 28. American Psychosomatic Society. Page 198, issue of February 1.
April 28. Alumni Association, Long Island College of Medicine. Page 458, issue of March 22.
May 7–11. National League of Nursing Education. Page 384, issue of March 8.
May 8. New England Society of Anesthesiologists. Page 512, issue of September 28.
May 9. Norfolk District Medical Society. Page 629, issue of October 19.
May 10. Differential Diagnosis and Treatment of Poliomyelitis. Dr. Louis Weinstein. Pentucket Association of Physicians. 8:30 p.m. Haverhill.
May 16. New England Obstetrical and Gynecological Society. Hillcrest Country Club, Leicester, Massachusetts.
May 16–18. American Association of Genito-Urinary Surgeons. Page 160, issue of January 25.
May 21–25. International Society of Orthopaedic and Traumatic Surgery. Page 422, issue of March 15.

District Medical Societies

HAMPSHIRE
May 2. 4:30 p.m. Annual meeting. Jones Library, Amherst.

NORFOLK
April 24. Boston Medical Library. 8 Fenway. 8:00 p.m.
May 9. Annual Dinner.

Calendar of Boston District for the Week Beginning Thursday, April 19

Thursday, April 19
*9:00–11:00 a.m. Medical grand rounds. Joseph H. Pratt Diagnostic Hospital.

Friday, April 20
*9:00–10:00 a.m. Medical conference. Joseph H. Pratt Diagnostic Hospital.
*9:00 a.m.–12:00 m. Combined medical and surgical staff rounds. Peter Bent Brigham Hospital.
*10:00 a.m. Surgical clinic. South End Health Unit, 57 East Concord Street, Boston.
*12:00 m.–1:00 p.m. Pediatric clinicopathological conference. Joseph H. Pratt Diagnostic Hospital.
*1:30 p.m. Tumor clinic. Outpatient Department, Mount Auburn Hospital, Cambridge.

Saturday, April 21
*9:00–10:00 a.m. Surgical grand rounds. Joseph H. Pratt Diagnostic Hospital.

(Notices concluded on page xv)